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CEREBRAL AND SPINAL MANIFESTATIONS OF PURPURA HÆMORRHAGICA

THE cases which are to be presented illustrate one of the rarer manifestations of purpura hæmorrhagica. Though it is unusual, hemorrhages are known to occur into the brain, the spinal cord, and cerebrospinal meninges, particularly in cases of idiopathic purpura hæmorrhagica. Pratt, in a series of 194 cases of idiopathic purpura which he collected, found that cerebral hemorrhage was the cause of death in 4 cases. During some observations upon patients suffering with diseases of the blood-forming organs both at the Pennsylvania Hospital, in Philadelphia, and the Presbyterian Hospital, in New York, 4 cases of purpura hæmorrhagica have been observed in which hemorrhages affecting the central nervous system and its membranes have occurred, and 1 case has been found in the records of the Presbyterian Hospital in which it is possible that a similar disturbance accounts for some of the symptoms which were present. All of these cases except one should be classed among the group of purpura hæmorrhagica. The one exception was probably an instance of aplastic anemia, in which the purpuric lesions were the most prominent feature.

CASE I

E. W., female, aged twenty-six, was admitted to the Presbyterian Hospital on July 9, 1919, complaining of headaches of

two weeks' duration, weakness of three months' duration, and nosebleeds of three months' duration. There was no history of any bleeding in the family. Except for swelling of her legs, feet, forearms, and hands, which appeared two years ago and persisted for two or three weeks, she had always been perfectly well. For three months she had been having nosebleeds every two or three days, which lasted for about ten hours. About one week after these started she began to feel weak. About three weeks before admission her gums began to bleed. Ten days before admission she woke up and was unable to see anything but a ball of fire with her left eye. Right eye seemed to be normal. The blindness in the left eye gradually improved and almost entirely cleared up. Twelve days previous to entrance into hospital she started to have headaches which were worse at night. She had been short of breath on exertion and she had had considerable palpitation. Until five months ago her menstrual periods had been regular, lasting about five days. Since that time they had persisted for seven days and the last two have continued ten days and have been very profuse. She has had no vomiting of blood, no spitting of blood, and has passed no blood in the urine.

Physical examination showed a very pale young woman who looked quite sick. There were blood crusts upon the external nares and upon the lips. The skin was almost lemon colored and thickly studded with petechial spots, varying from 1 to 3 mm. in diameter. In the left sclera there was a bright red hemorrhage. The eye-grounds were pale and the retina studded with numerous small hemorrhages, which were more extensive in the left fundus. The tongue was coated. Buccal mucosa showed a few scattered hemorrhages, and over the gums there were many hemorrhages, and the teeth were in poor condition. There was no rigidity of the neck. There was a hum over the jugular veins in the neck. There was a systolic murmur over the pulmonic area. The knee-jerks were somewhat diminished and there were no abdominal reflexes. An examination of the uterus showed that it was filled with organized blood-clots. It was slightly enlarged and soft, but in normal position.

6/21/19—Blood count: R. B. C., 3,000,000. Central pallor of red cells.
Hgb., 40 per cent.
W. B. C., 5500. Some aniso- and poikilocytosis.
Polys., 57 per cent. No nucleated reds seen.
S. lymph., 27.
L. lymph., 12.
Baso., 4.
Blood grouping: Group II.
Blood Wassermann: Alc. = negative. Cholest. = —.

6/23/19—Blood tests prior to transfusion:
Blood-platelets = 320,000 { Palmer method. / Hemoglobin = 32.33 per cent.
Reticulated red blood-cells = 1.5 per cent. Count made on 8 oil-immersion fields and average taken.
Red cell fragility test in saline solution.

	Patient.	Control.
Hemolysis began at	0.46	0.43
Hemolysis complete at	0.3	Not complete at 0.3
Coagulation time	13 min.	6½ min.

Not hastened by calcium.
Bleeding time = definitely increased over normal—no definite time taken. Observations made on skin punctures by needles.
Transfusion given at 8.45 P. M.—300 c.c. of blood introduced into vein of left arm. A reaction with chill, fever, and vomiting followed one-half hour after transfusion. This lasted about twenty minutes, but was relieved by adrenalin and Magendie solution.

On June 24, 1919, vaginal digital examination showed a third retroversion and a mass 4 to 6 cm. in diameter, ovoid, indistinctly outlined, slightly tender, firm, closely adherent to the uterus, free from pelvic wall in right fornix. On June 26th there was less bleeding from the teeth. Patient was somewhat nauseated, and was still passing blood-clots from the vagina. On the 27th she seemed much weaker and was complaining of numbness in the right hand. Cerebration was slow and seemed difficult, so that she answered questions with a great effort. She was quite drowsy. On the 30th 500 c.c. of blood were transfused. On July 1st she seemed somewhat better. Fresh purpuric spots appeared on the arms and neck. Less bleeding from the uterus. Hemoglobin, 35 per cent.; R. B. C., 2,000,000; percentage of reticulated blood-cells, 3. Blood-culture showed no growth of bacteria. On the 5th of July hemoglobin was 35

per cent.; R. B. C., 1,700,000. On the 7th a second transfusion of 500 c.c. was given. On this same date a dark bloody stool was passed. On July 8th hemoglobin was 45 per cent.; R. B. C., 2,500,000; W. B. C., 5600; polymorphonuclears, 62 per cent.; small lymphocytes, 20 per cent.; large lymphocytes, 15 per cent.; eosinophils, 1 per cent. Patient appeared somewhat improved. Early the next morning she complained of severe pain in her eyes and then a severe headache. Her pulse dropped from 105 to 50. There was profuse bleeding from the nose and vagina and she vomited both old and fresh blood. Her condition grew rapidly worse, and she became unconscious and died on the morning of July 9th. During her illness her temperature had been somewhat irregular, varying between 100° and 103° F., pulse-rate had been rapid, running from 100 to 130. Blood-pressure was usually about 110 systolic and 60 diastolic. The urine showed heavy traces of albumin, with great numbers of red blood-corpuscles, probably a contamination from vaginal bleeding.

Autopsy on E. W.—Autopsy was performed on July 9, 1919, by Dr. R. F. E. Stier.

Petechial hemorrhages were found in the skin, over the peritoneum, through pericardium, through the lungs, in the stomach, rectum, vagina, and urinary bladder. Some of these hemorrhages were quite large, being 0.5 cm. in diameter. The cervix of the uterus was of a deep purplish-black color and from the external os protruded a blood-clot. The uterine canal was filled with blood-clot and the entire endometrium appeared necrotic.

There was fatty degeneration of the heart muscle and of the liver.

The lungs showed a bronchopneumonia.

Both the ureter and pelvis of the right kidney were greatly dilated.

Examination of the brain was as follows:

"Beneath the dura mater, covering the left temporal and parietal lobes, there is a diffuse, hemorrhagic area in which there is fibrin and fresh clots. This clot measures 10 cm. in diameter

and is 0.5 cm. thick. The cerebral cortex beneath this hemorrhage shows a brownish-yellow pigmentation. Over the right temporal lobe, the lower portion of the frontal lobe, parietal and occipital lobes there is a diffuse, subpial hemorrhage. There escaped from the right temporal lobe, when the brain was removed, a blood-clot which measured 3 cm. in diameter and around

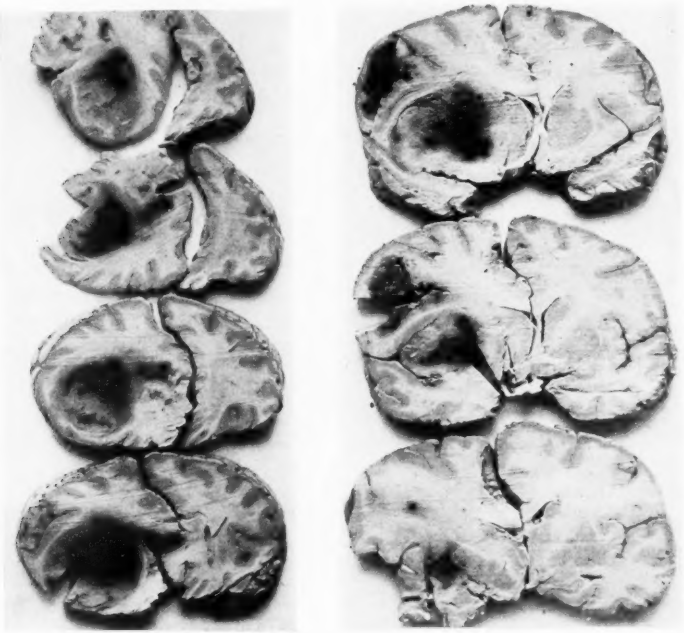

Fig. 61.—Photographs of horizontal sections of brain showing size and extent of hemorrhages into right temporal and occipital lobes.

which the brain tissue is fragmented. All of the brain structures of the right temporal lobe are very friable and easily broken. Sections of the brain show a large hemorrhage measuring 3 cm. in diameter, involving the entire portion of the right temporal lobe, which around the brain tissue is diffusely infiltrated by smaller hemorrhages. These large hemorrhages in-

volve practically the whole right temporal and occipital lobes (Fig. 61).

"*Microscopic Examination.*—Brain shows marked congestion and large hemorrhages into the brain substance. The brain tissue shows a vacuolization in many areas. The brain cells show no change. Section of dura shows a large subdural blood-clot."

Discussion of Case I.—This patient probably represented a characteristic instance of idiopathic purpura hæmorrhagica, although it is difficult to exclude some infection of the endometrium as a possible cause of the condition. The disease ran a rapid course and was unaffected by the transfusions of blood. In view of the extensive retinal hemorrhages it is probable that these accounted for the blindness in the left eye, and that this condition was not due to the hemorrhage into the brain. The symptoms of the cerebral hemorrhage developed late in the disease—evidently the immediate cause of death. As may be seen from the photograph there were two hemorrhages of fairly large size which involved practically the entire right temporal and occipital lobes, together with a diffuse subpial hemorrhage over the right temporal lobe, the lower portion of the frontal lobe, the parietal, and occipital lobes.

CASE II

G. G., aged twenty-two, Italian laborer, was admitted to the Pennsylvania Hospital, Philadelphia, service of Dr. J. C. Wilson, on June 24, 1908, complaining of chills and fever, pain in the abdomen, and pain in the throat. He gave no history of any previous illnesses. While at work, twenty days ago, he suddenly had a fainting spell with pain in his throat. Following this he had chills and fever and abdominal pains. Physical examination showed that he was well built, but looked somewhat emaciated. The mucous membranes and skin were sallow. He was constantly spitting up a thin bloody sputum. Tonsils were dark red and swollen and showed white patches. The spleen was enlarged. There were numerous irregular ecchymotic spots on the skin of the arms and thorax and over the thighs. Pulse was 108.

June 26th blood count showed R. B. C., 860,000; W. B. C., 3200; Hgb., 20 per cent.; P. M. N., 20 per cent.; S. M. N., 66 per cent.; L. M. N., 4 per cent.; bas., 1.6 per cent.; undeter., 2.4 per cent.; coagulation time four to four and a half minutes. The red cells were fairly regular, though many were microcytes. No nucleated R. B. C. No polychromatophilia or basophilic granulation.

June 28th blood count showed 3500 leukocytes; P. M. N., 22.4 per cent.; S. M. N., 68.8 per cent.; L. M. N., 6.4 per cent.; l. baso., 1.2 per cent.; undeter., 0.8 per cent.; baso., 0.4 per cent.

June 30th, blood count taken fifteen minutes before death showed R. B. C. 444,000; the white cells stained very poorly, red cells stained fairly regularly, and were not very pale. When varying in size they were smaller than normal. No polychromatophilia, no basophilia, no nucleated reds. Urine contained faint traces of albumin and granular casts. Patient became rapidly worse. Temperature varied between 101° and 103° F. and pulse between 108 and 136. Tonsils became necrotic. He continued to spit up large quantities of bloody sputum and the purpuric spots increased in number. Cultures from the throat showed no diphtheria bacilli. Death occurred on June 30th.

The autopsy showed purpuric spots over the skin of the chest, arms, and legs. There were small hemorrhages over the serous surface of the peritoneum. The epicardium of the heart was sprinkled with bright red hemorrhages, and hemorrhages were likewise seen scattered through the endocardium. The heart muscles showed fatty degeneration. Over the pleura there were small petechial hemorrhages. There was one hemorrhage in the right lung. The spleen was slightly increased in size. Over the mucous membrane of the stomach there were numerous hemorrhages, some of which were confluent. The bone-marrow was bright yellow and seemed to be almost entirely composed of fat. The brain was of moderate size. The dura was delicate and not adherent to the pia. The color was pale. Over the cortex the sulci were well marked. At the tip of each of the temporal lobes there were irregular bright red hemorrhages about 2.5 cm. in diameter. In the pia a third one was seen,

somewhat farther back on the left side. On section, these hemorrhages were found to be confined to the membranes. The cerebellum was wonderfully speckled with bright red minute hemorrhages. On section, the gray and, to a less extent, the white matter showed the same remarkable speckling of tiny red

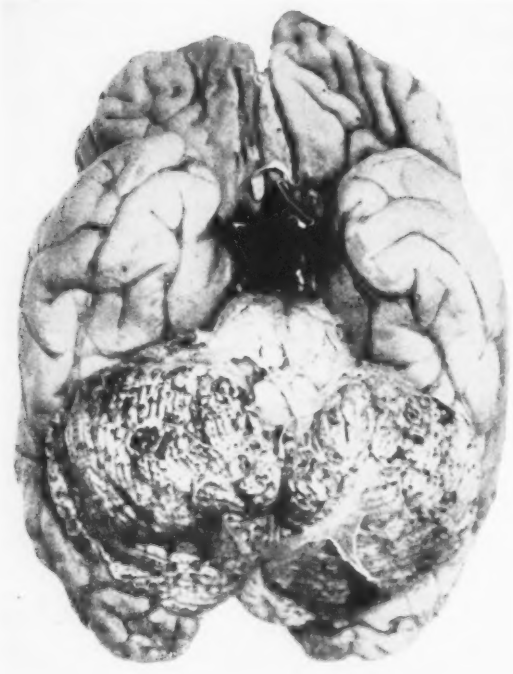

Fig. 62.—Photograph of under surface of brain, showing hemorrhage in and beneath the pia at the base of brain and multiple small hemorrhages in the cerebellum.

hemorrhages, which were round and just about the size of a fly speck. The cut section looked as if it had been covered with brilliant red fly specks. The brain on section showed here and there both in the white and in the gray matter a few of the petechial hemorrhages seen in the cerebellum (Fig. 62).

Microscopic examination of the meninges and brain showed the cerebral and in places the cerebellar meninges to be filled with blood, and in the cortex of the cerebrum and cerebellum there were numerous small hemorrhages. There was no infiltration of cells.

Discussion of Case II.—The case which has just been described presents some difficulties in accurate diagnosis, since it is possible that purpura might be considered as secondary to the tonsillar infection, or that the patient was actually suffering from an aplastic anemia complicated by a tonsillar infection and by a severe form of purpura. The extremely fatty bone-marrow and the rapidly progressing anemia are in favor of the latter diagnosis. The progress of the case was rapid and the anemia which developed was of an extreme degree. The total leukocyte count was also low and the differential count shows a relative lymphocytosis. The presence of the hemorrhages which are shown in the accompanying illustration were not suspected during life and were found only at autopsy.

CASE III

I. J., male, aged thirty, American, admitted to the Pennsylvania Hospital, Philadelphia, January 4, 1911, service of Dr. Norman Henry. He was admitted unconscious. It was learned that previously he had been complaining of bleeding from the gums and the nostrils. When he was twenty years of age the tonsils were removed, after which he had such a severe hemorrhage that it could hardly be controlled. His family had noticed that during the summer he had become pale. Three weeks before admission he suddenly fell to the floor unconscious and had to be put to bed. In about five or ten minutes he regained consciousness and was able to move about, but felt very weak. Fully a month previous to this he had been bleeding slightly from the nose and the gums. Following the fall the patient vomited dark green fluid. During the last week he had been extremely irritable and had had a ravenous appetite. The day before admission he became unconscious.

Physical examination showed a poorly nourished, somewhat

emaciated man. There was internal strabismus of both eyes and a small hemorrhage in the sclera of the left eye. He could not be aroused, but would move the arms and legs if pricked with a pin. He was extremely pale. There were signs of hemorrhage over the gums and lips. Over the abdomen, chest, and legs were many fine petechial hemorrhages. Many fine crepitant râles over the lungs, posteriorly. Abdomen held somewhat rigidly. Liver and spleen could not be felt. There was no facial paralysis. Knee-jerks were greatly exaggerated and there was a double ankle-clonus and a positive Babinski reflex. Blood count showed 7900 leukocytes, P. M. N. 48.3 per cent., lymphocytes 48.3 per cent., mono. 1.6 per cent., transitionals 1.3 per cent., basophils 0.3 per cent., hemoglobin 14 per cent.

The prick made to obtain blood for the count oozed for three-quarters of an hour. Urine showed a faint trace of albumin—no casts. Patient died within twenty-four hours after admission to the hospital.

The autopsy disclosed hemorrhagic areas over the skin of the arms, with a sprinkling of petechial hemorrhages over the abdomen and thorax. Over the diaphragmatic pleura there were extensive ecchymotic patches. Pericardium contained 150 c.c. of slightly blood-tinged fluid, and over the visceral pericardium there were numerous irregular ecchymoses. Beneath the endocardium there were extensive hemorrhages and a few small hemorrhages were scattered through the heart muscle itself. The lungs showed bronchopneumonia on the left side. Spleen was small. The mucosa of the urinary bladder was heavily sprinkled with numerous small hemorrhages. In the mucosa of the cecum and colon there were ecchymotic patches, the largest of which measured 2 mm. in diameter.

"Brain: The skull appears normal and there are no abnormal adhesions on the dura. Between the dura and the pia there is a small thin, dark red clot measuring 2 to 3 cm. in diameter. The pia over the cortex shows occasionally a small ecchymotic area, but for the most part appears normal. The convolutions are pale gray. At the base of the brain around the optic thala-

mus and the circle of Willis beneath the pia there is a rather marked suffusion of blood. No point of rupture is found in any of the arteries. The sixth cranial nerve where it emerges from the pons is surrounded by a slight amount of extravasated blood. Over the cerebellum there is a very marked condition of subpial ecchymoses, the whole cortex of the cerebellum being splattered with small areas of hemorrhage. On section, there are seen small hemorrhages beneath the pia between the cerebellar convolutions and also in the cortex. A few scattered hemorrhages are also seen in the white matter. Section of the brain shows everywhere the same condition. Occasionally small ecchymotic points are seen in the gray and white matter of the cortex. These are found also through the basal ganglia and are probably more marked in the walls of the lateral ventricles. The same condition is found in the medulla. The hemorrhages, however, are very small and scattered through the substance of the brain, while over the surface of the cerebellum they are especially numerous.

"Microscopic examination of the brain: In the sections of the brain there is seen an occasional very small area of hemorrhage in the cerebrum and brain stem. In the cerebellum, however, the hemorrhages are larger and more numerous and occur both beneath the pia and in focal areas through the brain tissue."

Discussion of Case III.—Case III was, as far as could be determined, one of characteristic purpura hæmorrhagica. On admission to the hospital the history led one to suspect a cerebral complication, inasmuch as the patient had had one attack of unconsciousness from which he recovered. Examination revealed besides the total unconsciousness, strabismus and exaggerated reflexes with the double ankle-clonus and bilateral Babinski reflex, which led to the conclusion that he had had some process affecting the upper motor neurons. The cerebral hemorrhages discovered at autopsy confirmed this suspicion of some lesion of the brain.

CASE IV

E. S., aged twenty-two, admitted last to Presbyterian Hospital March 5, 1919. Epitome: Chronic purpura. Under ob-

servation since 1908, with repeated subcutaneous hemorrhages, epistaxis, bleeding from gums, melena, and hemorrhages from bowels. During last admission signs of meningitis with bloody spinal fluid.

Patient was admitted first to the Medical Ward of the Presbyterian Hospital on January 4, 1908, with a diagnosis at that time of hemophilia. His mother had had heart trouble and was living; father was living and well. There was no history of bleeding in any members of the family. He did not use alcohol or tobacco. He ate well; bowels were regular. Had been rather robust and active up to the last two or three years. He had measles and scarlet fever as a child. Present illness started about five years ago, when, following the extraction of a tooth, there was persistent bleeding. Previous to this, however, he had had frequent epistaxis, lasting from one to eighteen hours, in one or two of which attacks he was obliged to be in the hospital. On several occasions during the last five years there had been blood in the stools. Small hemorrhages in the skin over all the body were almost constant occurrences and were often precipitated by the slightest trauma. When he scratched himself the bleeding was profuse. There had been no hematuria, no joint pains, no abdominal pain. About four months before admission he had over a period of three weeks three severe nosebleeds. On admission the hemoglobin was 40 per cent., R. B. C. 3,432,000, and coagulation time eleven minutes. When he was discharged on February 14th hemoglobin was 65 per cent., coagulation time five minutes. From May 21st to June 1, 1908, he was quite well. On May 27th coagulation time was one minute, hemoglobin 80 per cent. On June 2d he had a fairly severe epistaxis. On April 18, 1909, he was again admitted to the hospital, this time to the surgical wards, complaining of spitting of blood. He looked very pale, teeth were in fair condition, although there was oozing of blood about the roots of the upper teeth. Over the left arm there was a large ecchymotic area, 10 by 8 cm. in diameter, and one over the sternum, 6 by 3 cm. Several other smaller ones were observed over the arms, hands, and thorax. Hemoglobin was 80 per cent., R. B. C. 5,300,000,

W. B. C. 29,500, 84 per cent. polymorphonuclears, 11 per cent. lymphocytes, 3 per cent. transitionals, coagulation time nine and a half minutes. During his stay in the hospital he had a few more ecchymoses and some epistaxis, which was stopped by adrenalin applied locally. On January 19, 1911, he was again admitted with a moderate epistaxis, which was stopped by the nasal applications.

On July 16, 1913, he came to the hospital with an infection of the right hand. This time there were numerous small ecchymotic spots all over the skin of the body. There was also a blowing systolic murmur at the apex of the heart. The abscess of the hand was opened, following which there was a bloody oozing from the wound for about eight days. Between this time and January 4, 1916, he continued to have repeated epistaxes which, however, were not of very long duration, lasting only ten to fifteen minutes, whereas they used to last from four to five hours. About February, 1916, he had severe nosebleeds which continued off and on for two days. Later he noticed blood on the pillow when he wakened in the morning. He had frontal headaches, chills, dizziness, and had become dyspneic on climbing stairs. He continued to have the hemorrhages all over the skin. Occasionally he had noticed fresh blood in the stools. After he had had a severe nosebleed he has sometimes vomited blood, which he thinks he has swallowed. Appetite poor. Has had no other bleeding, no dimness of vision, no edema of his feet. At time of admission he seemed quite well developed and well nourished, but very pale. Scattered over the neck and chest there were several petechial hemorrhages. Besides these petechial spots there were large purpuric areas 1 to 2 cm. in diameter scattered over the chest and thigh. All the superficial lymph-nodes were readily palpable. Gums were soft and there were blood-clots about them, while many of the teeth margins showed fresh bleeding. Tonsils were large and soft, pharynx was red, and scattered over the pharynx and uvula were many small petechial spots. Lungs were clear. Heart impulse was in the fifth space, 6 cm. from the midline. There was a soft blowing systolic murmur at the apex transmitted to the axilla.

This became quite loud over the pulmonary area. The spleen was not palpable. The deep reflexes were normal. Eye-grounds showed no hemorrhages. A complete hemotologic history of this patient is given later.

At this admission the anemia was quite severe. It was found by blood grouping that he belonged to Group II. Resistance of the red blood-corpuscles to hemolysis in saline dilutions was normal, hemolysis beginning at 0.44 per cent. sodium chlorid and becoming complete at 0.36 per cent. Test made at the same time upon the control blood gave exactly the same figures. Blood was present in the stools. On January 13th a count of the blood-platelets gave 132,000. On January 15th the bleeding time, performed by the method of Duke, was twenty-three minutes. On January 19th the blood-platelets were 144,000. During this admission the patient was transfused with citrated blood on two occasions, but during his six weeks' stay in the hospital his condition was little improved, though the anemia on discharge was not so marked as may be seen from the table. On the 2d of February, just before discharge, the blood-platelets were 180,000. He returned again on February 29th for another transfusion. At this time the blood-platelets were 176,000. During his stay in the hospital there was no fever, and pulse-rate varied between 75 and 100. The blood-pressure was 120/60. Urine showed no albumin, no casts, and no urobilin. On March 16, 1919, the patient was again admitted to the Presbyterian Hospital. He was at this time twenty-two years of age. Since his last admission to the hospital he had been quite well except that the epistaxes had continued every one to four weeks. The general improvement had continued until about two weeks ago, when he caught a bad cold, followed by headaches. A little later his throat became sore. About a week before admission he started to vomit. For three or four days he had been nauseated constantly and had vomited four or five times a day. The vomitus early in the morning would contain blood. His bowels had been constipated in spite of large doses of cathartics. He had had no blood in the stools. General physical examination was much the same as those made previously. There were

ecchymoses and petechiæ all over the skin about the lips, and the gums were bleeding. Temperature varied between 98° and 100° F. Examination of the central nervous system showed somewhat exaggerated deep reflexes. There was some slight stiffness of the neck and there was a definite Kernig sign. The patient seemed extremely ill, was greatly excited, and was difficult to control. The abdominal pains were very severe and there was almost continuous vomiting. Blood was present in the stools. On the 7th, in spite of the high blood count, a transfusion was given. On the 10th the blood-platelets were 72,000. By the 17th he had improved and was able to take soft diet. About the 26th of March the patient became again greatly excited and complained of burning pain in the sides of his abdomen. His abdomen was held quite rigidly on examination. He also complained of some weakness in his legs. On March 29th there was some fever and a gradual increase in the pulse-rate. By April 2d the pulse-rate was 120 and the temperature about 101° F. On this date it was noted that the neck was particularly stiff and Kernig's sign was very marked. Some meningeal involvement was suspected and a lumbar puncture was made. At this puncture thick bloody fluid came through the needle. During the next month the patient was extremely ill. The temperature varied between 99° and 102.5° F., the pulse-rate between 100 and 130. The stiffness of the neck increased and Kernig's sign became more marked. He was delirious during most of the time. There were no marked changes in the deep reflexes and no Babinski could be obtained. During April, 1919, there was gradual improvement, and a transfusion of 250 c.c. of citrated blood was given on April 16th. During the next month improvement gradually continued. Temperature and pulse-rate came to normal. Stiffness of the neck and Kernig's sign gradually disappeared. Bleeding from the gums ceased and by June 1st the patient was up and walking about. He left the hospital in as good physical condition as he had been in for several years. He was last seen in September, 1919, when his condition was about that observed previous to his last admission to the hospital.

TABLE SHOWING BLOOD COUNTS IN CASE IV

Date.	W. B. C.	R. B. C.	Hgb. per cent.	Coagulation time.
1/4/16	6,600	2,200,000	70	
1/5/16	8,500	2,400,000	40	
1/6/16				6 min.
1/10/16		2,000,000	40	
1/17/16				11 min.
1/19/16				6.5 control Prothrombin time Patient Control. Optimal time 9½ min. 9 Minimal time 12 min. 13 Antithrombin time Optimal time 9 min. 8 Minimal time 11½ min. 8½
	(before transfusion)			
1/21/16	5,000	2,900,000	42	
	(after transfusion)			
1/23/16	8,400	2,960,000	45	
1/31/16	14,800	3,200,000	42	
2/5/16	7,200	3,200,000	46	
2/9/16	5,200	2,720,000	38	
2/10/16	18,000	3,500,000	45	
2/11/16	17,400			
2/14/16	12,000			
2/29/16	7,500	3,600,000	40	
3/1/16	10,200	3,520,000	45	
3/7/17	17,000	6,850,000 (?)		
3/7/19	Transfusion			
3/8/19		6,050,000	90	
3/10/19	Transfusion			
	16,200	6,100,000	90	
3/12/19		5,200,000	90	
3/12/19		5,784,000	85	
4/3/19	16,000			
4/4/19		3,800,000	60	
4/4/19				Control, 6.5 min. solid clot. Blood of patient—10.5. min.
4/4/19	20 c.c. normal horse-serum given.			
4/4/19				Patient's, 8½ Control, 8¾
4/7/19		4,700,000	50	
4/8/19				11¾ 11
4/11/19	20,000			
4/15/19	21,600	5,600,000	65	
4/23/19	17,000	4,500,000	60	
5/3/19	10,000			
5/5/19		4,232,000	60	
6/2/19		4,264,000	60	
7/1/19	8,800	4,152,000	55	

Discussion of Case IV.—Case IV was of particular interest, since this patient had been studied over a long period of time and represented a characteristic case of chronic purpura hæmorrhagica. The signs of meningitis which developed and the presence of bloody spinal fluid which was obtained on lumbar puncture leave little doubt that there was in this instance a hemorrhage either beneath the pia at the base of the brain or somewhere in the spinal meninges. The prognosis at this time was necessarily extremely grave, but the case demonstrates the fact that such hemorrhages may occur, from which the patient recovers completely.

CASE V

R. F., male, American, aged sixteen, factory hand, was admitted to the Presbyterian Hospital September 15, 1918, complaining of vomiting for four days and pains in the joints. He had never had any serious illnesses before. Nine days before admission he felt weak, had pains in his knees, and some fever. By the third day of his illness the pains and fever disappeared, but he had an epistaxis, after which he vomited. Since then he had been vomiting constantly. At the onset of the illness red spots appeared on the shins. The day before admission he had definite pains in the elbows. Upon examination he was found to be a poorly nourished boy, appearing quite sick. There was dry blood in the nostrils. The heart and lungs were normal. Spleen was not palpable. There was some pain on attempting to flex the right elbow and some soreness on deep pressure, but no swelling or reddening. Over the shins there were irregular, orange-colored splotches. Temperature was 101° F., pulse-rate 72, blood-pressure 125/90, R. B. C. 5,500,000, hemoglobin 70 per cent., W. B. C. 18,000, poly. neut. 73.5 per cent., eosin. 0.5 per cent., small lymph. 22 per cent., large lymph. 4 per cent.

On September 16th submucous hemorrhages were noticed in the posterior pharyngeal wall. The Wassermann reaction was negative. Urine was of 1026 spec. grav., showed traces of albumin, and contained numerous red blood-cells. Blood urea on September 18th was 0.31 gm. per liter. Excretion of phthalein in two hours was 58 per cent. On September 20th—leukocytes

17,000, polymorphonuclears 65 per cent., large lymphocytes 35 per cent.

By September 21st patient seemed somewhat worse. The temperature was 102° F., pulse-rate had increased to between 90 and 110. New crops of hemorrhages had appeared in the skin. The neck was stiff and there was a slight Kernig's sign. There were no changes in the knee-jerks and ankle-jerks. During the next few days the spots continued to appear. Three blood-cultures showed no growth of bacteria. On September 24th lumbar puncture gave 8 c.c. of clear fluid which flowed without increased pressure. There were 9 cells per cu. mm., globulin +, Wassermann negative, and culture sterile. During the next few days the stiffness of the neck and the Kernig's sign decreased. On October 1st there was blood in the stools. The blood count at this time showed 70 per cent. hemoglobin, 3,300,000 red blood-corpuscles. On October 1st he complained especially of abdominal pain, and in the afternoon he passed a stool containing bright red fluid blood. Condition remained about the same, with fever and fairly rapid pulse. On October 2d hemoglobin 60 per cent., R. B. C. 3,500,000, W. B. C. 20,500, polymorphonuclears 71 per cent., eosinophils 1 per cent., basophils, 0, small lymphocytes 26 per cent., large lymphocytes 2 per cent. Transfusion of 500 c.c. of blood given. On October 15th there again developed rigidity of the neck, with Kernig's sign. Knee-jerks at this time could not be obtained. Patient was complaining of severe headache and was quite irritable. Eye-grounds were normal. Lumbar puncture on October 17th showed clear fluid under increased pressure. There were 200 cells per cu. mm. globulin +. No bacteria obtained in growth. On October 18th there was slight weakness of the left upper eyelid and the pupils were unequal. Some spasticity of the arms was also noted. On October 23d the patient suddenly threw the right arm into the air, keeping it stiff and rigid, and clenching teeth, having what the nurse thought might be a mild epileptic convulsion. Examination immediately afterward showed no weakness, no stiffness of the neck, no changes in the reflexes. Optic disks were normal. On October 25th the patient was considerably better, complaining

only of slight abdominal cramps. The temperature and pulse-rate were both lower. By November 1st the patient was distinctly better, temperature was normal, pulse-rate 85, and from this time on convalescence was rapid and uneventful. On November 15th R. B. C. were 5,200,000, W. B. C. 12,200, polymorphonuclears 70 per cent., large lymphocytes 22 per cent., small lymphocytes 8 per cent., hemoglobin 70 per cent. During his entire stay in the hospital there was albumin in the urine, varying from a trace to a very heavy trace, with occasional red blood-cells and quite constantly hyaline and granular casts. The specific gravity was usually high, from 1020 to 1030. The urine was acid.

Discussion of Case V.—Case V presented a picture of purpura with joint and abdominal symptoms, and although there is no positive proof that the symptoms and signs which led to the suspicion that the patient was developing meningitis were due to hemorrhage into the brain or into the arachnoid spaces, there is evidence to show that some abnormal process had affected the meninges, since in the spinal fluid from both lumbar punctures globulin was present, and in the second there was a pleocytosis of considerable degree. The stiff neck, Kernig's sign, slight ptosis, and muscular spasticity were therefore associated with an irritative process in the meninges, and possibly in the cerebral cortex itself.

It might be suggested as an explanation for these findings that small hemorrhages had occurred in the cortex of the brain or in the cerebellum similar to those pictured in the illustration of the brain from Case II. Under these circumstances symptoms of meningitis together with the slight generalized and focal signs described might occur and yet the spinal fluid might only show an evidence of inflammation, but no signs of hemorrhage into the membranes.

Though gross hemorrhage of the brain or into the cerebrospinal meninges is not very common in purpura, the literature contains descriptions of considerable numbers of cases. Perhaps one of the most noteworthy articles on the subject is that

of E. Wagner.[1] In an extensive review of this entire subject, with the report of many cases illustrating the different types of purpura, he describes 8 instances of hemorrhage into the brain or its membranes. In one there was a pachymeningitis with fresh hemorrhage in the subdural space. In the second instance an extensive fresh subdural hemorrhage was found without any evidences of previous chronic inflammation of the dura. In the third case the bleeding was subpial. In 5 other fatal cases there were principally numerous fresh hemorrhages into the brain substance itself. The symptoms and signs in these cases varied according to the site and size of the hemorrhages. In some, headache, coma, or epileptiform convulsions occurred. In others there were more direct, localizing signs. The commonest among these was hemiplegia. In 2 cases it was noteworthy that there was a slow and progressive paralysis of one side beginning in the face, extending to the upper extremity, and later to the lower extremity. From rather frequent observations which he has made upon cases of purpura Wagner suggests that small hemorrhages may occur with eventual recovery. He describes one such case in a boy of five who suffered from a chronic purpura with frequent vomiting of blood. From time to time there were rather severe cerebral manifestations which simulated very closely an early meningitis, and were accompanied by high fever. Each attack lasted only three or four days, after which recovery was perfect. The second case, which occurred in a man of twenty-two, was one of purpura of rather short duration. The patient presented suddenly one evening well-marked psychic disturbances with inability to recognize visible objects. This condition cleared very rapidly. Six days later the patient had a general epileptiform convulsion. Twenty days later he died. The autopsy showed a hematoma of the dura mater with old hemorrhages into the brain.

Sir William Osler in his articles upon the Visceral Lesions of Purpura and Allied Conditions[2] classes in one group those cases with cerebral manifestations. He records 2 cases in which re-

[1] Deutsch. Archiv. für Klin. Med., 1886, vol. 39, p. 431.
[2] Brit. Med. Jour., 1914, vol. i, p. 517.

curring attacks of hemiplegia occurred in patients who were subject to attacks of urticaria, angioneurotic edema, colic, purpura, and hematuria. To explain these transient hemiplegias he suggests that there is a temporary edema of the cerebral meninges similar to the subcutaneous localized edema. In this connection I have seen one case of serum disease following the use of antidiphtheric horse-serum in a woman at the University Hospital in Philadelphia, in which at the onset of the severe generalized urticaria there appeared a temporary hemiplegia affecting the face, arm, and, to a less extent, the leg. It is highly probable that in this instance the transient paralysis was dependent upon local edema of the meninges similar to the swelling in the skin caused by the giant urticaria. Sir William Osler further describes 3 cases of coarse hemorrhage into the brain as a manifestation of purpura hæmorrhagica.

Apparently the hemorrhages in these cases of purpura may occur beneath the dura, in the cerebrospinal meninges, or in the substance of the brain, cerebellum, or the spinal cord, and may vary from the size of a millet seed to large hemorrhages covering the greater portion of one hemisphere or involving the substance of several lobes of the brain. As a rule the hemorrhages are multiple and it is not possible to discover a bleeding vessel. The symptoms may vary greatly in the different cases. Hemiplegia is perhaps the most common phenomenon. Occasionally single groups of muscles may be paralyzed, as occurred in Case III. In another group convulsive seizures occur as the only manifestation of the cerebral lesion. The fatal convulsion may be followed by coma or coma may suddenly develop without previous epileptiform convulsions. In the third group meningeal symptoms are those which attract most attention. This is best illustrated in Cases IV and V. In such instances it is probable that a small hemorrhage occurs in the membranes at the base of the brain or into the spinal meninges. It is likewise possible that such symptoms may arise in cases where several minute hemorrhages are scattered through the cortex or the cerebellum. Under these circumstances the mechanical injury is analogous to that which occurs in true encephalitis. The occurrence of

bloody spinal fluid in Case IV led to the correct diagnosis in this instance. Except from absolute necessity one hesitates to make a lumbar puncture in a case of purpura hæmorrhagica, for fear that some slight injury to vessels might produce a serious hemorrhage into the spinal meninges, but should the symptoms of meningitis become severe, it is believed that the lumbar puncture is highly justified and may, from relief of pressure, sometimes be of actual therapeutic benefit. It might be advisable before a lumbar puncture is performed in these cases to give a transfusion of blood, so that every precaution may be taken to prevent further bleeding into the meninges.

Summary.—Five cases of purpura are presented to you for consideration. In one death occurred from multiple large hemorrhages into the cerebrum; in two cases death occurred with diffuse hemorrhages into the subarachnoid space combined with great numbers of small hemorrhages into the cortex of the cerebrum and into the cerebellum. In one case there was hemorrhage into the spinal meninges, with recovery after lumbar puncture, and in the fifth case the symptoms and signs of meningitis, together with ptosis and spasticity of the muscles, were associated with high cell count and increased reaction for globulin in the spinal fluid. It is suggested that this last patient, who made an uneventful recovery, had had during the attack of purpura hæmorrhagica a few hemorrhages into the substance of the central nervous system combined with irritation of the meninges, but without hemorrhage into the subarachnoid space.

CLINIC OF DR. LEO BUERGER

MT. SINAI HOSPITAL

CYSTITIS

Discussion Regarding Its Therapy

IN a previous clinical talk[1] I ventured to enter into a critical discussion of the validity of the appellation "cystitis" when applied by the practitioner to the symptom-complex usually regarded as indicative of bladder inflammation. Many of the clinical pictures so frequently confused with cystitis were alluded to in support of the contention that, with the proper agnostic attitude toward the nature of so-called cystitis on the part of practitioners, and a more intense desire to obtain an exact anatomic diagnosis, much suffering may be prevented, and the lives of some patients may be saved.

Today it is my purpose to present for your consideration merely some of those fundamental principles so well known by the expert urologist, but little heeded by the internist by reason of intensive thought in other directions—principles that when properly estimated and weighed may lead to a better comprehension of the treatment of that great multitude of lesions commonly designated and included in the general name of *cystitis*.

Every rational method of treatment when applied to cystitis must presuppose a knowledge on the part of the medical man of the pathologic processes with which he has to deal. That such knowledge in the case of the bladder must needs remain concealed to a great extent is due to his inability without special cystoscopic training to have any visual concept of intravesical alterations. However, in spite of these difficulties, in spite of the concealed nature of the pathologic lesions, the

[1] Medical Clinics, 1919, p. 1055 et seq. (Saunders & Co.).

medical man can, by study, by occasional cystoscopic demonstration, by an intimate comprehension of the causal relationship between the supra- and intravesical urinary tract in the production of cystitis, obtain an adequate insight into the multiformity of inflammatory bladder processes; and will—when presented with a case—have at once in mind all those extravesical causes the treatment of which may be far more important than that of the bladder itself. Furthermore, he will be competent to set the indications for the application of the visual diagnostic methods (cystoscopy) as soon as occasion will arise.

A dependable, practical concept of the principles involved in the treatment of cystitis presupposes a much more thorough knowledge of pathology here than in the case of other diseases. For, when we are dealing with an inflammatory process of the pleura, or of the synovial membranes of the joints, there are comparatively few types of specific inflammation or of pathologic alteration that come into consideration. So also in inflammatory processes in other parts of the body. In the bladder, however, a most remarkable variety of microscopic and gross changes is to be encountered, either alone or accompanied by neoplastic formations. This is due to the fact that not only are we dealing with a viscus whose lining may be the seat of bacterial invasion, but with a cavity into which one of the body's most complicated excreta is deposited. In this sac the mechanical and clinical factors are often given to evoke complicating changes in the urine itself, leading to the deposition of abnormal chemical constituents, to the formation of calculi, and to the production of encrustations that cling with surprising tenacity to the mucous membrane of the bladder interior. Here is collected a fluid which when of abnormal composition may, in itself, give rise to irritative phenomena that may simulate in many particulars the so-called disease "cystitis." Not only by virtue of its function as a reservoir for one of the bodily excreta of complicated chemical composition but also by vitrue of its close anatomic relation with the kidneys and ureters above, and the urethra and the sexual adnexa below, is the bladder prone, by propagation from these, to suffer from a variety of extravesical maladies. By

reason of lesions at the bladder outlet, particularly in the male, are conditions produced that lead to the complications of retention, secondary urinary fermentation, chemical alterations in the bladder urine, and the elaboration of by-products that are just as formidable in their symptomatic manifestations as the changes in the bladder mucosa themselves.

In short, the question of the treatment of cystitis requires a knowledge of pathologic lesions as well as of the chemistry of the urine perhaps necessitating a more intimate study than do lesions elsewhere, since the bladder lesions may be the expression of—

(1) Inflammation by contiguity, and

(2) By remote extension from the kidneys and ureters, or from the prostate and urethra;

(3) Of inflammation associated with conditions that are of far greater importance than the cystitis, namely, tumor, stones, or ulcer;

(4) Of inflammation due to the irritative effects of abnormal chemistry of the urine in an impaired or vicious metabolism;

(5) Of inflammation by reason of obstructive conditions at the bladder neck (fibrosis of the sphincter, contracture of the neck, so-called hypertrophy of the prostate or adenoma);

(6) Of inflammation by extension from extravesical lesions (pelvic abscess, appendicitis, etc.), and

(7) Of inflammation by reason of congestive causes (in the rectum, constipation; in the sexual organs, onanism or excessive coitus; in the rectum, hemorrhoids, carcinoma, etc.).

Then, again, we must not forget that even were the types of cystitis confined to those inherent in the bladder itself, uninfluenced by supra-, infra-, or extravesical pathologic processes, there would still remain such a diversity of pathologic lesion as to warrant the conviction that no one method of treatment could apply; but that each case is worthy of special cystoscopic investigation, and with particular modification in therapy best suited to the clinical and pathologic complex under consideration.

The **treatment of cystitis** must be based upon the recognition of the type of disease present in any particular case. You will

ask, "Is there merely an inflammation of the bladder present, or is the bladder involvement secondary and but the manifestation of other lesions?" To lay down the *dictum* that a case with the symptoms of cystitis, be it chronic or acute, should receive certain well-recognized therapeutic procedures, would lead to an error in a great number of instances. For in the event of temporary abatement of symptoms in the acute cases, after general therapy and possibly bladder irrigations had been administered, the patient would be lulled into a sense of false security regarding his true condition, and would make no further attempt to have the cause of his so-called cystitis investigated.

The futility of the mere treatment of the bladder mucosa, be it with silver nitrate, argyrol, protargol, ichthargan, potassium permanganate, or what not, unless an accurate knowledge of the exact condition of the supravesical tract is at hand, is attested by numerous cases of infection of the renal pelves, the cases of pyelitis. It is because the lesion of the supravesical tract may be a latent one, because pain in either lumbar region may be absent, that the influence of the transmission of organisms downward by canalicular conduction may be overlooked.

CASE I.—*Latent Bilateral Pyelitis Without Symptoms; Symptoms of Cystitis Only, Therapeutic Indications Being Not Only Directed to the Bladder, But Also to the Renal Pelves.*

S. P., female, thirty-two years of age, consulted me on October 5, 1917. She began with an attack of hypogastric pain in August of the same year, with severe pain on voiding lasting a few days, followed by gradual abatement of the severity of the symptoms. Since then urgency, frequency, and pain have returned and continued with varying degrees of intensity up to the present day, so that she now has a desire to void almost every fifteen minutes. During the acute attack she had had a dull ache in the lower back, but since then no symptoms referable to this region had been noted.

Cystoscopy on October 5, 1917, showed a cystitis of moderate severity, and specimens from both kidneys were *almost clear*. Microscopic examination, however, showed pus-cells in both the right and left kidney specimens, and bacteriologic

examination demonstrated the presence of Bacillus coli communis in the specimens from the right and left kidney specimens as well as in the bladder.

In brief, we have here an exquisite demonstration of the value of appreciating the significance of supravesical (namely, ureteral and renal) infection, in its bearing upon the perpetuation of a bladder inflammation.

Concerning the Futility of Treatment of Cystitis when the Renal Pelvis is Involved.—So commonly does the urologist encounter cases that have been treated for weeks and months for symptoms of cystitis, when a cystoscopic examination would demonstrate the pelvis of one or both kidneys is involved, and so frequently are such patients allowed to develop destructive renal lesions by the nonchalant practitioner by reason of failure to institute topical applications into the ureter and renal pelvis, that it cannot be too strongly emphasized *that the treatment of the pyelitis is more important than that of the bladder, for the latter is more apt to take care of itself.*

CASE II.—*Cystitis Treated for Several Months with Irrigations, Latent Pyelitis Overlooked, Intense Pyelitis (Probably Pyelonephritis) Resulting, with Fever and Chills, Cured by One Application of the Cystoscope, the Ureter Catheter, and Pelvic Lavage.*

A. P., female, twenty-eight years of age, had been suffering for about five months from "cystitis." About five months ago she began to develop urgency and frequency of urination without cause. There had been no instrumentation, the appearance of the symptoms being wholly inexplicable to the patient. Bladder irrigation seemed to cause slight improvement, but the bladder symptoms always tended to return, according to the patient, with renewed severity. She consults me because of an extremely sharp pain during and following urination, and because four weeks ago she began to have fever and chills. However, *she believes that even at the beginning of her trouble she had a very definite although mild pain in her back.*

Examination on March 12, 1918, showed a diffuse cystitis, the specimens from the right kidney containing *numerous pus-*

cells, the function of the right kidney being slightly diminished, as attested by the output of indigo-carmin. There are numerous clumps of pus-cells in the right specimens. The left specimens are negative. The right kidney is palpable and distinctly enlarged.

Diagnosis.—Right-sided pyelitis, with cystitis, and enlargement of the right kidney.

Drainage of the right kidney pelvis with the ureteral catheter during cystoscopy, and lavage of the right pelvis. *x*-Ray examination on the same day was negative for calculus, the right kidney being slightly enlarged.

The patient was placed under observation at the New York Polyclinic Hospital and Medical School, and no further local treatment was given. *Immediate improvement occurred* after the cystoscopy. The right kidney was distinctly smaller on the following day and the bladder symptoms diminished.

March 16th (four days after cystoscopic treatment) the temperature was normal, having been 103° F. on admission, and the patient was discharged three days later with the urine almost clear, *all the symptoms having disappeared.*

What an exquisite example of the ineffectiveness of treating cystitis without cystoscopic aid, and how striking the value of emptying a distended and infected renal pelvis with the ureteral catheter!

The Importance of Clinical Diagnostic Methods in the Treatment of Cystitis.—With the above clinical evidence of the necessity for thoroughly appreciating the rôle of other parts of the urinary tract in mind, let us review what the practitioner himself can do toward arriving at a tentative diagnosis of the causative factor in any given case of cystitis. It may be asked, If cystoscopy is necessary in very many cases, when the acute symptoms have subsided, what is there left for the practitioner to do, and how is it possible for him without instrumental means to obtain even an approximate idea of the lesion?

However true it may be that the urologist may have to be depended upon in the final analysis, as the court of last resort, for a precise appraisal of the lesion in many cases, it is never-

theless well recognized that a careful evaluation of the history and a thorough investigation of the physical status may enable the practitioner in a large percentage of cases to acquire a fairly correct appreciation of the possibilities and probabilities in many cases of cystitis. How close to an exact diagnosis he may arrive will depend upon his clinical acumen and his knowledge of the most likely conditions in any given case.

Let me present to you in a sort of schematic way how this problem of tentative diagnosis, before cystoscopy is resorted to, may be approached.

In making your tentative hypothesis as to etiology and variety of lesion you will find it expedient to divide your cases into

(1) Males (adolescents, adults, old men).

(2) Females, and

(3) Children.

INVESTIGATION BY ANAMNESIS AND PHYSICAL EXAMINATION

In Adolescents and Middle-aged Men.—To have the characteristic etiologic and symptomatic data at your disposal for tentative diagnosis you will do well to inquire as follows:

(1) Has he had or has he recently acquired a gonorrheal urethritis?

(2) Has he or has he had prostatitis?

(3) Has he been treated for either one or both of these conditions?

(4) Have sounds or other instruments been passed through the urethra or into the bladder?

(5) Has masturbation led to the introduction of foreign bodies?

(6) Has a stricture of the urethra existed? Does it exist? Has he difficulty in voiding? Must he strain to empty the bladder, and is the act prolonged?

(7) Have operations been performed upon the urinary tract for stricture, prostatic abscess, or stone in the bladder?

(8) Have there been attacks of retention of urine preceded by difficulty in voiding?

(9) Have symptoms of pollakiuria, nocturia with clear urine

preceded the presence of the cystitis for a long time (possible contracture of the neck of the bladder)?

(10) Has the patient noticed an interruption in the stream during the act? Does he pass urine better in the erect position or in the dorsal decubitus? Does he have pain in the bladder when walking, when jolted, when running? Is there terminal hematuria (vesical calculus)?

(11) Does he notice that the bladder cannot be emptied during one act of micturition, but that there appears to be some residual urine which he can dispose of subsequent to the act, either spontaneously or by increasing abdominal pressure with the aid of the hand?

(12) Has he had a number of attacks of so-called cystitis, and has the last attack, or have possibly the last several attacks, been accompanied by marked terminal hematuria, blood appearing at the end of the act of micturition, with increasing pain at the termination of the act (ulcer or multiple ulcers, rarely carcinoma and tuberculosis)?

(13) Has he had painless hematuria in the past, with attacks of blood in the urine coming out without cause, unattended by any renal symptoms, disappearing without the aid of treatment, with larger amounts of blood at the end of the acts of micturition than during; and is there now associated a clinical picture of cystitis (papilloma or papillomata with superadded cystitis)?

(14) Has he had attacks of renal or ureteral colic; has the situation of the pain become progressively lower; has the pain extended along the course of the ureter; has it lately reached the region of the iliac fossa, and recently given rise to bladder symptoms (descending ureteral calculus arriving at or in the bladder); or following such a history of renal or ureteral colic, have intense urgency, frequency, difficulty in micturition, or even attacks of retention supervened without prior manifestations of bladder irritability (descending ureteral calculus impacted in the posterior urethra)?

(15) Has he had attacks of lumbar pain, dull ache in the lumbar region associated with fever, preceded by or associated with bladder symptoms (pyelitis, pyelonephritis)?

(16) Has there been lumbar ache for a long time, continuous or in attacks, with symptoms of the intermittent hydronephrosis; and have fever, associated with the symptoms of cystitis, been recently added (infected hydronephrosis and cystitis)?

(17) Has there been a history of pollakiuria, persisting for a considerable length of time, with or without hematuria, with nocturia, with or without lumbar ache, possibly albumin and later pus in the urine (tuberculosis of the kidney and of the bladder)?

(18) Has the patient been dribbling, has he lost control of his bladder to a certain extent, is he becoming incontinent, has there been lues (tabes, with infection of the bladder)?

(19) Is there chronic constipation (congestive cystitis due to constipation), with or without bacteriuria?

(20) Are the symptoms of strangulated or thrombosed hemorrhoids present (cystitis symptoms with or without inflammation of the bladder due to hemorrhoids)?

(21) Has there been cloudy urine for a long time, with previous attacks of frequency and urgency (bacteriuria, colon bacillus, Bacillus lacticus, Bacillus mucosus capsulatus, etc.)?

(22) Has the urine been cloudy, is the patient very neurotic, has he had attacks of urethritis, which have been diagnosticated as non-specific; does a milky fluid appear after urination, which on examination is shown to be not of prostatic origin (phosphaturia with cystitis)?

In short, certain strikingly characteristic historic data can be elicited in most cases, so that an approximate diagnosis can be arrived at, or at least the extravesical etiologic factors can either be wholly excluded or certain of them held responsible.

Tentative Diagnoses in Old Men.—Most of the interrogations above noted will apply here, but, in addition, we may also suggest:

(1) Has there been nocturia, without any noticeable increase in urinary frequency during the day; have there been attacks of retention of urine without indulgence in alcohol, without exposure or any noticeable cause (so-called hypertrophy, adenoma of the prostate with secondary cystitis)?

(2) Have diurnal and nocturnal frequency been present for some time; does the patient present albumin in the urine; is there high blood-pressure; is he said to have had angina? (With any one of these present, we may be dealing with a case of *fibrosis of the neck of the bladder*.)

(3) Has frequency been present for a considerable period of time, both diurnal and nocturnal; has there been increasing difficulty in voiding; have there been occasional attacks of hematuria or loss of weight; does rectal examination reveal a small, but very hard prostate (carcinoma of the prostate with infection)?

(4) Does the patient complain of *piles*, bleeding from the rectum; has he lost weight; has there been diarrhea; have bladder symptoms supervened with blood in the urine, or merely pus (*carcinoma of the rectum, with or without involvement of the bladder and cystitis*)?

Suggestive Clinical Data in Females.—(1) Is it the first attack of urinary trouble in a young woman recently married, with bladder irritability, frequency, cloudy urine (gonorrheal urethritis with cystitis; or Bacillus coli cystitis)?

(2) Has she had recurrent attacks of urinary frequency, brought on without cause, or after exposure or bathing in the surf (Bacillus coli cystitis)?

(3) Had any such attacks been preceded, associated with, or followed by ache in the lumbar regions or back, with fever (Bacillus coli pyelitis)?

(4) Had frequent attacks of mild cystitis disappeared, the urine becoming clear, but the urgency and the symptoms of the cystitis persisting (*trigonitis, cystitis colli or limited areas of leukoplakia trigoni*)?

(5) Has an attack of so-called cystitis persisted for a considerable period of time, is it associated with terminal hematuria, is the frequency so great that the patient can bear it no longer; is the nocturnal frequency particularly marked (ulcer of the bladder, (non-tubercular), or tuberculosis of the bladder and kidney)?

(6) Has there been a recent acute illness, pneumonia, influ-

enza, typhoid, followed by cystitis (postpneumonic, postinfluenzal, posttyphoid cystitis—also applying to men)?

(7) Has a gynecologic operation been performed recently, with or without catheterization?

(8) Are backache, metrorrhagia, and menorrhagia, striking symptoms, and have they been recently attended with intractable bladder symptoms (fibromyomata of the uterus with cystitis)?

(9) Had she borne many children, is there a prolapse of the uterus, cystocele, rectocele, with recurring attacks of cystitis (cystitis due to malposition of the uterus, relaxed vaginal outlet)?

(10) Has the cystitis persisted for some time, and has the family physician found difficulty in catheterization (*stricture of the urethra in females rare, but does occur*)?

In addition to these questions, some of those applying to men, particularly those in reference to primary renal infections, may here also be applicable.

Anamnestic Data to be Elicited in Children.—(1) Has the little girl had a vaginal discharge (gonorrheal cystitis, urethritis)?

(2) Was there an attack of pyelitis—fever, with or without any other symptoms, in early infancy, with cloudy urine—such attacks repeated subsequently—with symptoms of cystitis supervening (coli pyelitis and cystitis)?

(3) Has the child increasing difficulty in micturition, has it developed a chronic cystitis, is there occasional spastic incontinence or retention (bladder symptoms of cystitis accompanying spina bifida)?

(5) Is retention of urine a striking symptom, or has it been overlooked; is it associated with symptoms of cystitis, possibly accompanied with fever and lumbar ache; does the bladder urine contain pus and is there definite evidence of retention discoverable on palpation of the abdomen (congenital hydroureter, hydronephrosis, congenital obstruction at the neck of the bladder, spinal lesion or in cauda equina)?

(6) Does the child merely present symptoms of frequency,

nocturia, and pyuria with or without enlarged cervical glands, or glands elsewhere, with or without a palpably enlarged kidney (tuberculosis of the bladder and kidney)?

CONCERNING THE MANAGEMENT OF CYSTITIS

To present here a comprehensive discussion of the management of cystitis would lead me far beyond the scope of such a clinical lecture. May it suffice, therefore, if I invoke the aid of a few interesting clinical cases to illustrate how each and every form of cystitis requires its own particular method of therapeutic approach. Much can be done by the practitioner, however, even before cystoscopy is done, by anticipating the findings of the urologist according to the anamnestic scheme above described.

Inquire carefully as to whether an acute attack of cystitis is, in truth, of recent acquisition, or whether it be but an exacerbation of existing bladder symptoms, for it is only in this way that you will become suspicious of a possible tuberculosis of the kidney, and can judge correctly as to the right time for cystoscopic intervention. Impress upon each and every patient the necessity for more than merely conservative treatment after the first few days of rest in bed, fluid diet, alkalies, and the usual well-known remedies for acute cystitis have been resorted to. Acquaint him with the fact that unless you are certain of the cause of his cystitis, and are able to direct measures against it (as is the case in gonorrhea, hemorrhoids, stricture of the urethra, prostatitis, fibromyomata of the uterus, hypertrophy of the prostate, etc.), that a more profound and more grave lesion may be overlooked.

A few of the many forms of cystitis so readily recognizable by the expert cystoscopist should be known to every internist, both from the pathologic as well as from the diagnostic standpoint, so that he can co-operate with the specialist, and, if need be, take an active part in the treatment of the malady.

Let us, therefore, review some of the more important forms of cystitis, so that by a comparative study of the pathology,

prognosis, and known methods of medicinal and instrumental care a better concept of treatment may be acquired.

CONCERNING THE TREATMENT OF CERTAIN FORMS OF CYSTITIS

Bacillus Coli Cystitis in Women.—Although it may not be permissible to include under such a caption all the various forms of cystitis in which the colon bacillus may be a factor, it may nevertheless be pointed out that there is a group of cases occurring in the adult female where an inflammation of the bladder of various degrees of severity, without characteristic lesions, is brought about by the action of the colon bacillus, possibly when it has attained an unusual degree of virulence. For such cases it is advisable, after instituting the usual methods that have for their object the alleviation of the distressing symptoms, to give a course of bladder irrigations and in some cases topical applications.

Whenever possible, keep your patient in bed for a few days. Let her drink large quantities of pure water to which bicarbonate of soda is added in small doses; and, as for diet, be careful that all irritating and highly spiced foods, condiments of all sorts, be particularly prohibited. Try to restrain your patient from indulging in anything but cereals, milk, and toast for several days. Apply heat to the hypogastrium (suprapubic region), and in the male, because of the tendency to rectal spasms, hot rectal irrigations may be of value. As for medicinal treatment, alkalies, potassium citrate, and potassium acetate are of value; and for the tenesmus, opium and belladona suppositories or tincture of hyoscyamus should be resorted to.

Then, when the most intense symptoms have somewhat abated, the internal administration of internal antiseptics, such as urotropin (hexamethylenetetramin) with biphosphate of soda, or helmitol in 30- to 60-grain doses per day are to be administered.

This general treatment applies to all cases of acute cystitis, be it of the Bacillus coli variety or of other etiology.

In the Bacillus coli communis or communior cases in females

after the abatement of the acute stage we have found that daily irrigation with boric acid followed by the instillation of 100 c.c. of collargol in $\frac{1}{4}$ per cent. solution, increased gradually to $\frac{1}{2}$ or even 1 per cent., is an exceedingly valuable remedy. The boric acid irrigations must be very carefully carried out, particular heed being taken to avoid sudden distention of the bladder, overdistention, and production of vesical spasms. When the bladder is clean and the return flow is clear, from 50 to 100 c.c. of the collargol solution are injected carefully, and the patient

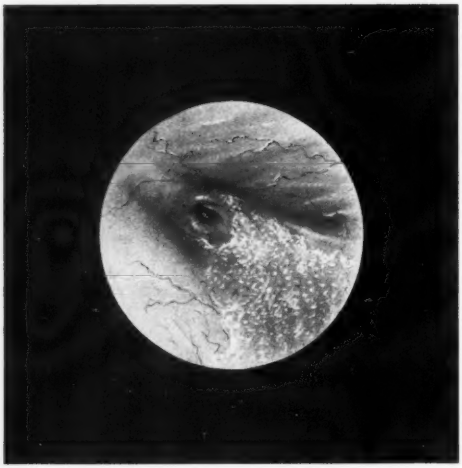

Fig. 63.—Veil-like exudate covering one horn of the trigone, and approaching the right ureter in a case of cystitis colli (due to Bacillus coli communis).

asked to retain this as long as possible. If no reaction occurs 100 c.c. may be used at the second injection, and this treatment repeated daily.

In other cases silver nitrate in solutions of 1 : 10,000, gradually increased to 1 : 3000, seems to be more advantageous, although it is more applicable to the subacute and chronic cases than to the acute form of infection. In other patients 25 per cent. argyrol is a valuable remedy.

Recurrent Cases.—For such cases it is particularly important

to seek the cause of the constant reinfection of the bladder with colon bacilli, and with this in view it is well to investigate the action of the bowels, to have a thorough bacteriologic and chemical examination of the stools made, to advise enemata if necessary, colon irrigation, laxatives, proper diet, and vaccines. Where the vaginal outlet is torn, where the urethra is relaxed, where other gynecologic conditions are present, the advice of a competent gynecologist should be sought, and many patients will be cured of recurrent attacks of cystitis when their pelvic organs have been surgically attended to.

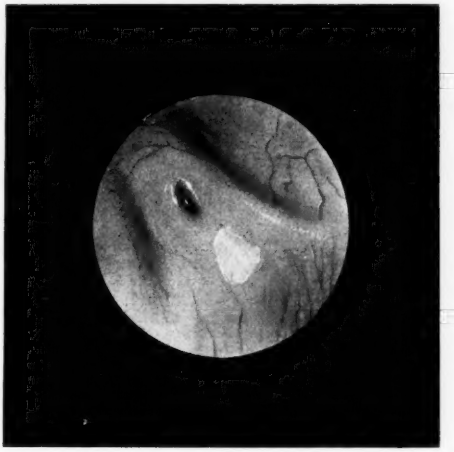

Fig. 64.—Sentinel exudate beyond the right ureteral orifice, being the residuum of a bladder inflammation associated with pyelitis.

Bacillus Coli Cystitis with Trigonitis with Cystitis Colli With or Without Renal Infection.—But it is the cystoscopist who will be able to enlighten you regarding those chronic changes that regularly make their appearance in the bladder when recurrences of this form of cystitis take place. A veil-like exudate begins to appear beyond one or both ureters, covering one or both cornua of the trigone, and may be regarded as significant and characteristic of a deeper pathologic lesion than that which attends

the simple acute case. Such exudate becomes adherent and is frequently a sentinel lesion indicative of an infection in the ureter and corresponding kidney (Fig. 63). Even small patches of exudate (seen in Fig. 64) can be demonstrated as characteristic sentinel lesions of a Bacillus coli communis infection of the renal pelvis.

In such cases lavage of the renal pelvis with 1 : 500 silver nitrate solution leads to striking cures in certain instances, while in others recurrences do not seem to be avoided thereby.

Cystitis Colli or Trigonitis.—This infection, characteristic of the female bladder, and often the outcome of previous attacks of acute cystitis, or an expression of uterine disorder, requires more vigorous attention and topical treatment on your part. Not only will it be necessary to treat the uterus, adnexa, and lacerations of the vaginal outlet, but stronger applications with 1 to 5 per cent. silver nitrate introduced on an applicator through an endoscope, repeated as occasion may require once or twice weekly, is a method that will give you gratifying results.

Intermediate Forms of Cystitis, Subacute and Chronic, Arising from Recurrences or Persistence of a Bacillus Coli or Other Infection.—Although you will be most gratified to see your cases of Bacillus coli cystitis (particularly in women) get well after the treatment I have outlined, there are others which, by virtue of renal complications, by dint of recurrences, repeated exposures, or reduced vitality, will either persist (as manifested by continuous cloudy urine containing pus) or go on to a more chronic form. Thus, while the lesions in the simple acute and subacute cases rapidly disappear, you will encounter others where the clinical history and cystoscopic findings go hand in hand in attesting to the profundity of the pathologic process.

Cystoscopic examination in such cases will reveal, in addition to the usual manifestations of recent inflammatory invasion, other stigmata of deeper involvement of the mucous membrane. Thus, in Fig. 65 a rather mild degree of such lesion is depicted, being taken from a case of recurrent Bacillus coli infection in a female. The trigone is swollen and reddened, the markings being practically effaced. The ureteral mounds are more prom-

inent than normal, and surrounded by velvety mucous membrane. The bas fond shows a most peculiar mottling, the surface of the mucous membrane having a honey-comb appearance, minute areas of deep red being interspersed with a network of slightly paler mucous membrane. Here and there are still further evidences of old trouble in the presence of tiny cysts and pustules, two of which can be distinctly discerned behind the right ureter, and a collection of such bodies lying near the left ureter in the illustration. It is the existence of such lesions

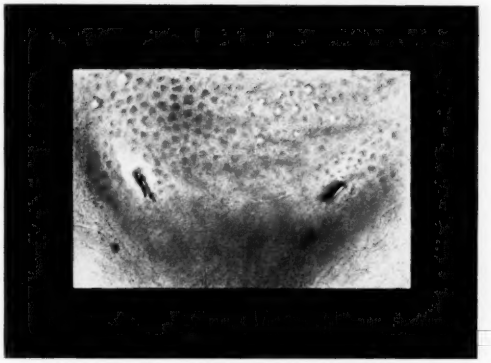

Fig. 65.—Bladder in a case of Bacillus coli infection in a female, showing mottling and marked congestion of the mucous membrane in the neighborhood of the ureteral orifices (honey-combed appearance) and tiny pustules of purulent cysts in the bas-fond.

that offer indications at times to the urologist for special topical applications or instrumental methods of treatment. So then you will remember that when the case does not respond to the ordinary methods, that you may be convinced that the pathologic alterations have attained not only greater extent, but greater depth in the mucous membrane, and that the chances for restitution to the normal are diminished. It is in these cases that you will have to have recourse to the methods of the cystoscopist, who by the recognition of such lesions may be able to apply the proper methods of treatment.

In recalcitrant cases the application of a high-frequency spark (fulguration) to the cyst and pustules will oftentimes aid in delimiting the progress of the disease, and in many instances bring about a rapid cessation of the symptoms.

Cases with Repeated Exacerbation.—Whenever you find a tendency to recurrence, or when a patient consults you with a history of having had repeated attacks, failure to ascertain the truth regarding the condition of the bladder and kidneys, the

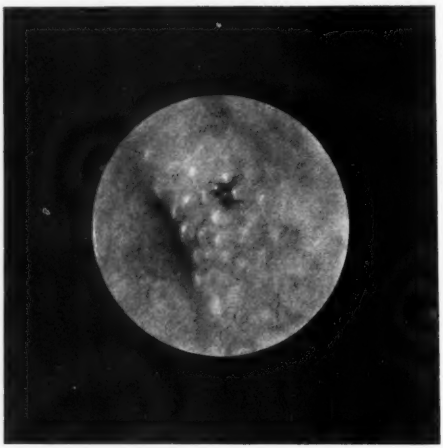

Fig. 66.—Cystoscopic picture showing distorted orifice in a case of chronic cystitis and Bacillus coli communis pyelitis; irregularity of the mucous membrane simulating the appearance of a raspberry surface.

sexual adnexa in the male, and urethra and pelvic organs in the female, will find its just retribution in your lack of success in the management of the case.

A glance at Fig. 66 with its portrayal of the region of the right ureteral orifice in a case of recurring cystitis in a male, with its striking reproduction of the distorted orifice, the swollen mulberry-like, velvety, angry red mucous membrane, will suffice to impress upon you the futility of treatment that does not take into consideration all the lesions, be they limited to the

mucous membrane itself or be they complicated by conditions in the ureter, kidney, urethra, or sexual adnexa.

Cystitis with Superficial Ulcerations.—While the occurrence of superficial defects in the mucous membrane is an attending pathologic lesion in many cases of cystitis, the presence of such ulcers is either an expression or a cause of the perpetuation of the clinical manifestations. It is these cases that are apt to be most unyielding to ordinary methods of treatment. The early application of the correct general as well as local methods of treatment in many instances by the practitioner may do much toward the prevention of their development. Careful clinical observations, the institution of the visual intravesical methods of attack in due time, as well as attention to extravesical lesions, may prevent the destruction of portions of the mucous membrane of the bladder and its deplorable consequences. Although many of these patients begin with a mild Bacillus coli infection, you will find later any of the pyogenic organisms, the Streptococcus hemolyticus, Micrococcus tetragenus, Bacillus lactis, Staphylococcus aureus (rarely), and even Gram-negative encapsulated bacilli belonging to the Bacillus ozænæ group.

When attacks of pyelitis and pyelonephritis complicate these conditions, the dejection, desolation, and mental suffering endured by some of these cases, particularly women, can be well understood.

CASE III.—*Chronic Cystitis, Pyelitis, Superficial Bladder Ulcer, with Varying Flora in the Bladder—Bacillus Coli, Bacillus Ozænæ, and Streptococcus Hemolyticus.*

A. L. S., female, fifty years of age, consulted me on April 5, 1915, because of a constant desire to void. She had had bladder trouble for more than a year, and since then has been very miserable. Potassium permanganate irrigations comprise all that she has had in the way of local treatment. She now has a constant desire to void, and gets up once or twice at night, the act being very painful.

Cystoscopy performed on April 5, 1915, reveals a markedly inflamed bladder, the mucosa markedly swollen. The whole of

the trigone, the bas-fond, and lateral walls of the bladder are involved and show characteristic surface changes. The vascular markings are absent over the entire diseased area, the greater portion being covered with exudate, although this can be washed off in parts, leaving grayish, linear shreds hanging on with great tenacity. Here and there plaques remain, indicating more intensive ulceration. The surface of the mucous membrane is irregular, having lost its smoothness, is edematous in many

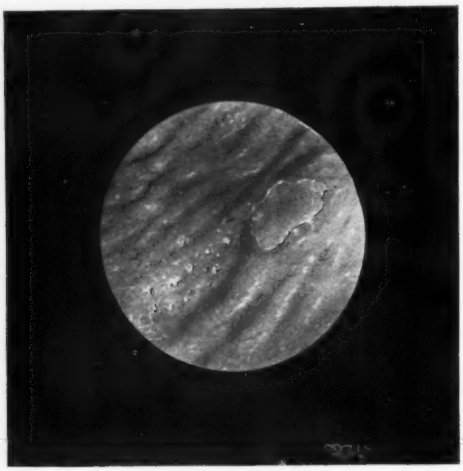

Fig. 67.—Cystoscopic view of a bladder in a case of chronic cystitis with a plaque of exudate over an ulcer, the exudate being exceedingly thin; fine shreds of exudate adherent in many places, the mucous membrane being folded in many places and hyperemic.

places, and is beset here and there with cystic bodies with flattened surfaces not unlike lesions of Molluscum contagiosum in the skin. Figure 67 depicts fairly well the irregularity of the mucous membrane, a superficial ulcer, and small patches of adherent exudate.

The kidney pelves showed evidences of infection.

It is the whole urinary tract in such cases that requires your attention, for such cases no longer have a bladder inflammation, but their ureters and pelves may be markedly diseased.

ULCERATIVE CYSTITIS (CHRONIC) REQUIRING SUPRAPUBIC CYSTOTOMY

One of the most intractable forms of inflammation of the bladder is that associated with multiple ulcerations, be they ever so superficial, when they have attained a certain degree of chronicity. These cases in their response to treatment vary considerably, and some are so recalcitrant that *suprapubic drainage may become necessary*. What other methods have we at our disposal for the cure of these ulcerative cases?

1. Direct topical application through a Kelly cystoscope or direct endoscope in the female;

2. Fulguration with the high-frequency current through the cystoscope;

3. Use of the retention catheter with frequent irrigations in the female; and

4. The usual bladder irrigations.

When these methods fail, suprapubic cystotomy must be done.

It must be understood, however, that a differential diagnosis between superficial ulcerations *without* and those *with* phosphatic deposits must be made, for the treatment of the former is quite different from the latter.

How beautifully some cases of chronic ulcerative cystitis yield to suprapubic cystotomy and drainage is demonstrated by the following case:

CASE IV.—*Chronic Cystitis of Eight Years' Duration (Ulcerative), Ulcerations on the Posterior Bladder Wall, Cured Within Four Weeks After Suprapubic Cystotomy and Drainage.*

B. L., female, forty years of age, mother of 6 children (referred by Dr. A. Reich), consulted me March 23, 1918, complaining of inability to hold her urine (spastic enuresis), some pain in the lower sacral and right lumbar region, intense burning and pain on urination, and marked increase of urinary frequency.

She has had bladder trouble for about eight years, when she began with burning on urination and increased frequency, without hematuria. The increased urinary frequency and inability

to hold her urine became progressively worse. About one year ago she developed some pain in the right lumbar region (pyelitis) and was admitted to the Polyclinic Hospital of New York where she was under observation for two weeks, cystoscopy being done, and the right kidney irrigated (pyelitis?). She was discharged at that time and is emphatic in her statement that "no relief was obtained."

For the last two weeks or more the pain on micturition has been so severe that it has become intolerable; she voids almost every fifteen to thirty minutes by day as well as by night. She thinks that her urine is so thick as to resemble "leukorrheal discharge." She has become very irritable and thinks that at times there have been chills and fever.

In short, a most characteristic history of suffering due to chronic bladder inflammation and ulceration.

Cystoscopy on March 23, 1918.—There is a diffuse cystitis, with numerous irregularly linear ulcerations to which shreds of exudate are attached. The left ureteral orifice looks as if it were punched out, has an irregularly crescentic shape, there being a total absence of the ureteral mound. The right ureter also shows ulcerations in its immediate neighborhood, and there are numerous superficial ulcers over the posterior bladder wall. There are a few follicular bodies that resemble tubercles.

Catheterization of the ureters shows that both kidneys are functionating well, the specimens from both kidneys containing a few red blood-cells, without pus.

Diagnosis.—Chronic cystitis with ulcers.

Examination for tubercle bacilli negative.

x-Ray examination negative.

Neurologic status negative.

No spina bifida.

Therapeutic Indications.—On March 27, 1918, I wrote to the physician that "in view of the fact that Mrs. L. has been suffering for so many years, I think that suprapubic cystotomy is indicated, since she has had no relief from conservative methods."

April 4, 1918, suprapubic cystotomy at the New York Polyclinic Hospital and Medical School. Exposure of the bladder

interior revealed very beautifully the very much swollen and inflamed mucous membrane of the posterior wall, and the superficial ulcers as well as the follicular bodies seen through the cystoscope. These had the appearance of being minute miliary abscesses in the deeper layers of the mucous membrane. The bladder mucosa was very much thickened, the bladder wall only slightly so. Because of the superficial nature of the ulcerations no cauterization was done, suprapubic drainage being carried out for sixteen days.

The patient made an uneventful recovery, bladder irrigation through the suprapubic drain being the treatment applied.

On April 20th the suprapubic drain was removed, and not reinserted, although another smaller drain had been previously substituted for the original large one.

Subsequent Course.—Within four weeks after the operation the patient voided slightly turbid urine, without pain, the intervals between the act being almost three hours.

On May 9, 1918, somewhat more than a month after the operation, she regarded herself as practically cured as far as bladder symptoms were concerned.

On May 14, 1918, less than six weeks after her operation, a cystoscopic examination was performed at my office, the ulcers having completely disappeared, the bladder being practically negative, the urine *macroscopically clear*, containing but an occasional pus-cell.

CYSTITIS CYSTICA AND PURULENTA AND ITS TREATMENT

There is a most interesting pathologic lesion that may involve the bladder alone, but also the ureters and pelvis of the kidneys which is known as *cystitis cystica*. In this we find numerous discrete or collections of small rounded vesicles occupying the trigonal region, the posterior wall of the bladder, or diffusely scattered over the whole bladder interior, being either true cysts filled with clear fluid, or being opaque, white or yellow, lying either in normal or in inflamed mucous membrane.

Originating in epithelial inclusions, the so-called *Limbeck* and *Von Brun's* crypts or glands, they may be indicative of mere re-

tention cysts, but when accompanied with an inflammatory process, they may become filled with pus, and act as a nidus for the continuance of the inflammatory intravesical process.

Figure 68 offers a good illustration of the reddened inflamed posterior bladder wall, harboring a multitude of such infected and non-infected cysts.

It would not be enough in such cases to attempt to rid the bladder of its inflammation by irrigations alone, but by means of the fulguration method with the electric spark an instanta-

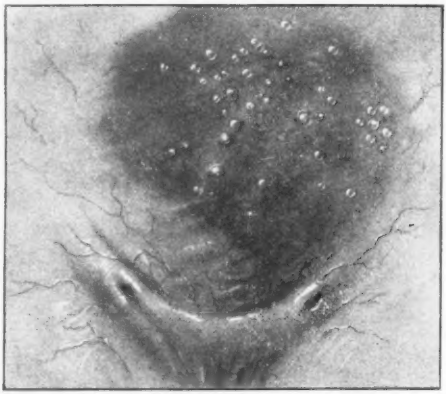

Fig. 68.—Lesions of cystitis cystica; behind the trigone the mucous membrane is represented by a darker area, there being numerous cysts filled with opaque yellowish-white material in this zone.

neous exposure of current is sufficient to rupture and destroy each cyst to which the applicator may be applied. Very excellent results may be obtained in this way.

CYSTITIS WITH PHOSPHATIC ENCRUSTATIONS. ENCRUSTED CYSTITIS

The term *encrusted* or *incrusted cystitis* may be employed to designate that large group of cases in which there is a most intensive liability to form deposits of phosphatic material or other salts in the bladder. Just as in phosphaturia, we very

frequently can observe large collections of phosphatic débris accumulate in the *bas-fond* of the bladder, and that these the patient may express at the end of the act in the form of a gush of milky fluid, so, in cases with an alkaline tendency, phosphatic

Fig. 69.—The working end of the author's punch forceps used for the removal of foreign bodies, pieces of tissue, and calcareous and phosphatic débris from the surface of ulcers in the bladder, etc.

Fig. 70.—The author's operating cystoscope with special operating forceps introduced.

and carboneous precipitation are apt to occur, in the presence of an inflammation, the tendency to coat superficial erosions, ulcerations with exudate and phosphatic and carboneous material, is greatly enhanced, and, indeed, goes on so rapidly that veritable stones may accumulate within periods of hours or days.

When such lodgments of chemical nature are of the flat or superficial type they form a type that is easily amenable to treatment with the author's operating cystoscope.

With the punch forceps (Fig. 69) introduced through the author's operating cystoscope (Fig. 70) the masses of precipitated and deposited salts are gradually removed, revealing, as a rule, a superficial bleeding ulcer.

Bladder irrigations with the usual antiseptic solutions are of little avail in these cases, and the following should be tried:

1. Treatment with the *Bacillus bulgaricus* injected daily after preliminary irrigation with boric acid, 5 c.c. of the *Bulgaricus bacillus* culture and 5 c.c. of a 5 per cent. glucose solution (pabulum) are mixed in a small glass, drawn up in a syringe, and injected into the bladder after the preliminary irrigation. This combination of solution and bacilli in broth is retained until the next voiding. Patients that are under observation at the hospital, particularly females, may receive more than one injection daily. The method depends for its results upon the ability of the *Bacillus bulgaricus* to overgrow other organisms in an acid medium, and to produce a considerable amount of acid in the presence of sugar. The acid developed prevents the deposition of salts, and the overgrowth of the Bulgarian bacilli crowds out pyogenic organisms.

2. Irrigations with 1 : 1000 hydrochloric acid solution, this being used with great care, the strength, amount, and frequency of application depending upon the reaction.

3. Irrigations with chloramin (Squibb's), in strength of 1 : 1000 to 1 : 600 daily, is of great value in some cases.

ENCRUSTED CYSTITIS WITH DEEP ULCERATIONS, PSEUDO-TUMOR MASSES OF SOLITARY ENCRUSTED ULCERS

In this type of disease, the lesions being much more extensive and profound, involving the mucosa, submucosa, and encroaching even upon the muscularis of the bladder, our therapeutic efforts will depend upon whether we are dealing with multiple encrustations (*a*) or solitary ulcers with pseudo-tumor formation (*b*).

CASE V.—*Encrusted Cystitis with Multiple Ulcers, Phosphatic Calculus, Submucous Inclusions Unimproved by Intravesical Methods, Cured by Suprapubic Cystotomy and Curetage and Excision of the Affected Areas.*

I. O., age forty-seven, male, referred to me by Dr. Louis Duke on March 3, 1919, has been voiding bloody urine for *four years*, micturition being associated with intense burning in the perineum. There has been urinary frequency almost four times an hour, nocturia four to five times, and exquisite pain at the end of the act. In spite of all that his practitioner and some specialists could do in the way of local treatment, no improvement has occurred. Some time previously he is said to have had a small tumor (?) over the trigone, which had received treatment by the fulguration method at the hands of a cystoscopist.

On March 3, 1919, *cystoscopy* demonstrated an exceedingly intense cystitis, the bladder being covered over a large extent by a grayish-white exudate, deposits of salt, the masses being of so great amount that a good view of the bladder could not be obtained.

Per rectum, too, the bladder is indurated, so that the possibility of carcinoma had to be considered.

Diagnosis.—Extensive encrusted cystitis, possibly concealing a neoplasm, and contracted bladder.

Although suprapubic cystotomy was urged, the patient refused to have this done, and, with bladder irrigation, the use of the Bacillus bulgaricus, argyrol, and other means, his condition slightly improved. However, his pollakiuria, urgency, and nocturia continued, and, on August 3, 1919, after five months of suffering, he again consulted me complaining of pain in the perineum, hypogastrium, occasional hematuria, marked urgency and burning, with increasing pollakiuria, both diurnal and nocturnal.

Cystoscopic examination revealed a small phosphatic stone, and over the trigone and in the *bas-fond* a number of areas of *encrustations*.

Suprapubic cystotomy was again urged, and the patient

finally acquiesced, so that on September 4, 1919, I performed a *suprapubic cystotomy* at the Mt. Sinai Hospital, the following being the findings:

The posterior wall of the bladder had a distinctly verrucous appearance, its surface irregular, intensely reddened, and inflamed. Behind the trigone there was a large zone of polypoid edema, an expression of chronic cystitis, without any evidence of infiltration or new growth. In the *bas-fond* a calculus of the phosphatic type, about 1 cm. in diameter, was removed with a forceps. Over the right half of the trigone there was an area of phosphatic incrustations, in the form of a ridge of salts and exudate so intimately adherent to the musosa that a curet had to be employed to remove it. Over the left posterior border of the trigone another irregular linear mass of incrustations was found to be so firmly attached and to extend so deep into the submucosa that excision with the scissors had to be resorted to for its removal.

Superficial curetage of a number of other areas of incrustations and suprapubic drainage were then carried out.

Within a few days the urine passing through the drain was clear, and after two weeks the drainage-tube was removed, the patient making an uneventful recovery.

Three and a half weeks after the operation *the urine was clear, and the patient considered himself cured.*

In short, a most remarkable cure after excision and curetage in the deep form of encrusted cystitis, in a man who had tried every other means known to the practitioner and specialist over a period of more than four years.

CYSTITIS REQUIRING THE TREATMENT OF EXTRAVESICAL CAUSES

Enough has been said of the treatment of certain forms of cystitis to emphasize the importance of diagnosticating renal lesions to make clear that irrigation of the pelvis of the kidney may alone suffice in restoring an inflamed bladder to normal in certain cases and to affirm the necessity for early nephrectomy when tuberculosis of the kidney has been discovered as being responsible for the bladder condition. It may still be worth

while to call attention to a very few lesions in the lower urinary tract, the recognition of which may lead to a cure of many cases of cystitis. Of the many such lesions, let us merely mention the following:

1. Hypertrophy of the prostate.
2. Fibrosis of the neck of the bladder and contracture of the neck of the bladder (and median bar).
3. Urethrocystitis with edematous and cystic lesions in the neck of the bladder and in the posterior urethra (usually post-gonorrheal).
4. Papillomata, particularly papillomata of the neck of the bladder, and
5. Urethral stricture.

HYPERTROPHY OR ADENOMA OF THE PROSTATE

While the possibility of an obstruction at the neck of the bladder by reason of mere neoplastic formation, in the shape of

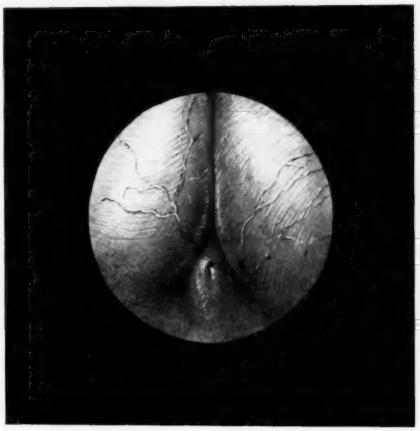

Fig. 71.—View of enlarged lateral lobes in so-called prostatic hypertrophy (viewed with the cysto-urethroscope).

submucous adenomata (so-called hypertrophy), will not escape you in the case of an elderly male, the absence of an enlargement

per rectum with the symptoms of *prostatism* complicated with cystitis, may fail to arouse the suspicion of "hypertrophy of the prostate," should a young or middle-aged man present himself for examination. It must be remembered that precocious development of adenomata in this region is not unusual, and we have at our disposal a most excellent means of inspecting their presence with the use of the author's *cysto-urethroscope*. When well developed, the adenomata usually present themselves in the form of two rounded bodies, and occupy the posterior urethra between the sphincteric region and the verumontanum, as seen in Fig. 71, the verumontanum being crowded down and insignificant in size. But even the most minute submucous and sphincteric hypertrophies or adenomata may be recognized by means of this instrument. Strange to say, very slight intravesical intrusions, when they occupy the region of the internal margin of the sphincter, may, when present in an irritable individual, or complicated with cystitis, give rise to cystitis of intractable nature. The ablation of such adenomata by the suprapubic route (suprapubic cystotomy) will bring about a cure.

CONTRACTURE OF THE NECK OF THE BLADDER

So important is this group of cases and so little is known regarding them by the surgeon as well as practitioner that I deem it wise to make mention of them here, so that you may take their existence into consideration, when brought face to face with cases of intractable cystitis. When you know that not only the symptoms of cystitis with clear urine may be mimicked by this condition but also that secondary cystitis such as will not respond to treatment is frequently a sequence of this pathologic process, the importance of its recognition and cure will become clear.

We may apply the general term "contracture of the neck of the bladder" to designate all those pathologic processes involving the region of the internal vesical sphincter, and the adjacent peri-urethral tissues of the prostatic urethra, that do not belong to the class of true neoplastic formation, and that result in a greater or less coarctation, rigidity, or distortions of this portion

of the urethrovesical canal. The fibromata or adenomata that may be located in this region are usually grouped in the category of so-called "hypertrophy of the prostate," although, correctly speaking, "fibro-adenomata of the prostate" would be a better appellation. When these latter are unaccompanied by fibrotic and inflammatory lesions leading to stenosis of the vesical sphincteric ring, they make a variety quite distinct from what we wish to term "contracture of the neck of the bladder."

It was the pathologic study of cases that gave the clinical symptoms of contracture of the neck of the bladder, cases that did not belong to the class of adenomata, that led me to adopt a more extensive operative procedure, than those which merely have for their purpose the removal of a small portion of tissue from the floor of the sphincteric region. These pathologic investigations on material obtained by a wide exsection of tissue from the affected region have brought me to the conclusion that although no single lesion may occur to make up the complex of contracture of the neck of the bladder, nevertheless, the anatomic alterations which lead to the narrowing of the bladder outlet are so extensive and deep that the radical surgical procedure suggested should give better results than some of the methods applied heretofore.

My pathologic studies have brought to light that we are dealing here with a combination of single lesions in some cases; others, however, representing invasion of the sphincteric and peri-urethral tissues extending far beyond the mucous membrane. These lesions may be a *simple fibrosis* of the sphincter without evidences of a previous inflammatory process, the fibrosis being of a varying depth, or there may be fibrosis accompanied by an inflammatory process, or there may be submucous and peri-urethral *inflammatory lesions* involving the sphincteric region and posterior urethra extending centrifugally for a variable distance into the surrounding tissues, forming an inflammatory fibro-scerlotic sheath of varying thickness; or there may be a *diffuse glandular invasion* of the sphincteric region with or without peri-acinar inflammation associated with more or less sphincteric fibrosis; and finally, there may be *mixed forms* in which any of

the above changes may be accompanied by the accidental formation of small adenomata or fibromata.

A critical analysis of the dignity of all the elements concerned in the pathology of each of our own cases, however, has enabled us to come to certain conclusions that are somewhat at variance with the observations of those whose investigations are based

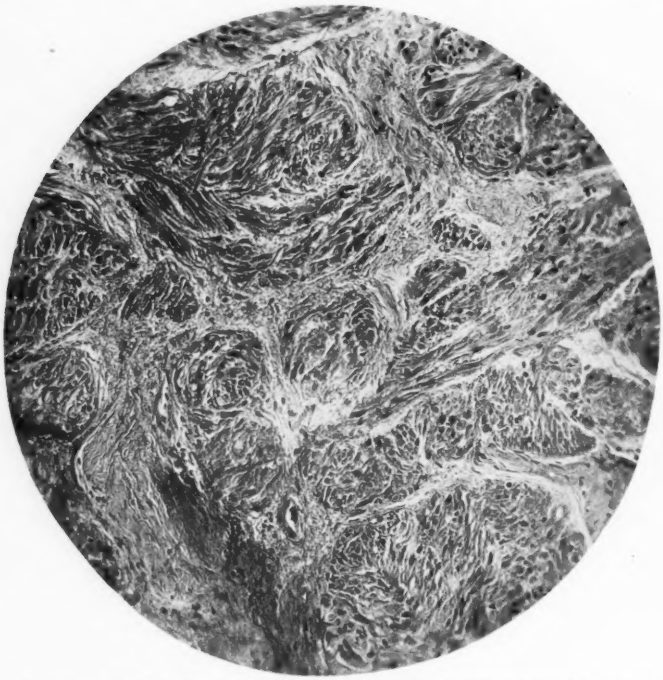

Fig. 72.—Photomicrograph showing fibrotic lesion in contracture of the neck of the bladder. (Section from author's case.)

for the most part on autopsy material. Although such work as that of Randall and the anatomic studies of Lowsley are exceedingly valuable in demonstrating beyond peradventure that vesical obstructions other than the pure adenomata and so-called hypertrophies frequently exist, nevertheless, our own clinical findings of other authors, who report true stenosis of a fibrotic

nature at the internal urethrovesical outlet. Other forms have been encountered, all having this in common, that an essentially fibrotic or inflammatory fibrotic lesion occupying the internal vesical sphincter and peri-urethral intraprostatic region is always present, even though accompanied by other changes.

Fig. 73.—Acute and chronic inflammatory lesions in contracture of the neck of the bladder. (Section from author's case.)

A simple and satisfactory pathologic grouping divides the cases into three classes:

1. Fibrosis (Fig. 72).
2. Fibrosis and inflammation (Fig. 73).
3. Fibrosis associated with adenomata or fibromata, or with infiltrating adenoma (Fig. 74).

The Fibrosis.—At operation, with the bladder opened suprapubically, we encounter the following evidences of regional alterations in and about the internal sphincter:

Visually, the striking abnormalities are an unusually small internal vesical orifice, and the presence of a horizontally situated transverse prominence (median bar) in the situation of the

Fig. 74.—Combined diffuse infiltrating adenomatous lesions with fibrosis in contracture of the neck of the bladder. (Section from author's case.)

postero-inferior lip of the sphincter, neither of these being essential for the existence of a contracture of the neck of the bladder, since the latter may occur in the form of extensive and diffuse rigidity of the sphincter and prostatic portion of the urethral channel, the sphincteric ring being seemingly patent. When a bar is well developed it may be exaggerated by edema,

by enormously congested capillaries and veins, it may involve merely the floor of the vesical orifice or extend laterally for varying distances, in some cases being truly eccentric and almost laterally placed.

Often a distinct shortening of the sagittal trigonal distance, with transverse plication of the retrosphincteric area will be appreciated, a furrow separating this interureteric bar from the vesical orifice. When the median bar is well developed or when edema and marked vascularization are intense the aspect of a congested and inflamed vaginal cervical ostium is simulated.

The tip of the index-finger introduced into the internal vesical orifice finds a hard, infiltrated, annular band or fibrous ring, effectually preventing its introduction into the urethra, and when force is employed, the engagement of the posterior urethra is at once followed by tearing of the outlet, most frequently at the roof of the neck.

Where the coarctation of the sphincter is but slight or doubtful, the tissues of the posterior urethra as well as the sphincter will be appreciated as having been converted into a fibrotic, hard sheath that reveals none of that resilience and elasticity so characteristic for the normal urethrovesical outlet. Or, in addition to these lesions, small areas of increased density may be palpated, these being manifestly due (as sections show) to multiple discrete fibromatous nodules.

Microscopically, you will find in the fibrotic cases (Fig. 72) a connective-tissue replacement of the muscle-fibers of the sphincter (Fig. 72), the process being diffuse, the muscle bundles being often widely separated by either dense or edematous connective tissue.

In the *inflammatory form* (Fig. 73) we note extensive inflammatory infiltration of the muscle, and the destruction of the sphincteric fibers, these being evidences of acute and subacute and chronic lesions, the intensity of the inflammatory and destructive process being beautifully shown in Fig. 73.

In the *mixed forms* there may be complicating adenomata, or there may be diffuse fibrosis, as in Fig. 74, complicated by infiltrating adenoma.

THE TREATMENT OF CONTRACTURE OF THE NECK OF THE BLADDER

With a view to relieving these stenotic sphincters and to enlarging the rigid inflammatory sheath the following simple operation that was devised several years ago by the author has been carried out with beneficial results:

The bladder neck is exposed (Fig. 75), the floor of the sphincteric ring is seized and elevated by a tenaculum forceps, and a **V**-shaped piece is excised from the sphincter. A pyramid is removed, the base of which is formed by a section of the bladder floor extending from the inferior sphincteric margin backward

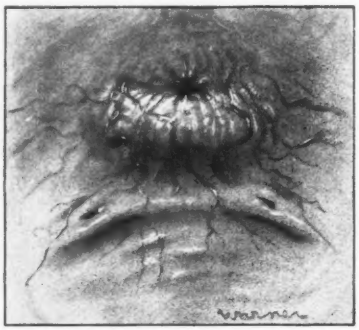

Fig. 75.—Contracture of the neck of the bladder, showing the tight orifice and median bar.

for 1 cm. along the apex of the trigone. Its lateral margin is delimited by the lateral margin of the sphincter, and the apex of this piece lies in the *fossula prostatica* (behind the verumontanum). The incision is carried downward into the prostate for at least 1.5 cm. through the sphincter. The finger is then made to enter the sphincter once more in order to dilate this as well as the supramontane urethra, a careful exploration being made for the presence of any complicating adenomatous or fibrotic neoplasm. Sounds are then passed through the urethra, the dilatation being carried to at least No. 32 French. If the bleeding is active a small packing may be placed into the sphincteric region

and posterior urethra, and carried through the suprapubic wound alongside the drainage-tube. When the bleeding is profuse it is best to place one or two catgut sutures into one or both lips of the wound area, inserting the needle so that the edges of mucous membrane are not brought together.

The operative results are excellent in these cases, at least 75 per cent. being cured.

URETHROCYSTITIS; ITS TREATMENT

Chronic inflammatory lesions about the neck of the bladder and in the posterior urethra, involving also the bladder, are not infrequently found in young men, and are most commonly the late results of a gonorrheal process (complicated at times with prostatitis).

Fig. 76.—Cystic lesion about the sphincteric region.

With the cysto-urethroscope cystic lesions are regularly encountered in the sphincteric region, encroach upon the trigone, and sometimes completely fill the posterior urethra behind the verumontanum, completely altering the verumontanum, which may be totally converted into a cystic body.

Figure 76 depicts the right margin of the internal sphincteric

region in a case of this sort, showing sausage-shaped, fusiform, and pyriform sessile bodies in an inflamed velvety mucous membrane. The recognition of this condition will lead to attack with the operating cysto-urethroscope, the cystic bodies being either punctured or destroyed by the fulguration method. Then the lesions in the posterior urethra are to be submitted to the usual methods of treatment. Through-and-through irrigations of the urethra with protargol, argyrol, and potassium permanganate and silver, followed by gentle prostatic massage, together with the instrumental method above described, constitute the most effective therapeutic means of completely eradicating the lesions.

PAPILLOMATA OF THE BLADDER AND NECK OF THE BLADDER

Although papillomata are at times associated with infection of the bladder, particularly when they are multiple, this is more

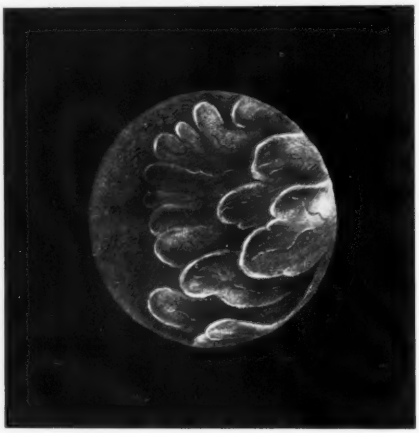

Fig. 77.—Papillomatous tufts at the sphincter, enlarged because of proximity to lens of the instrument, and floating, as it were, in the bladder fluid.

frequently the case with papillary carcinoma. The existence of papillomata, however, is not so likely to be overlooked when they lie in the bladder itself, but when they occupy the region of the sphincter (Fig. 77) they may even escape observation with the

cystoscope, the latter pushing them aside. With the cysto-urethroscope some of the villi (Fig. 77) and the pedicle in the sphincter and urethra may be more readily detected in this region so difficult of access. They should be destroyed with the fulguration method, either through the author's cysto-urethroscope or through the convex sheath of the author's catheterizing cystoscope.

STRICTURE OF THE URETHRA IN MALE AND FEMALE

The rôle played by stricture of the urethra in the production of a severe cystitis is not sufficiently appreciated, as evidenced by my case files, which contain numerous instances where a stricture has been overlooked, the diagnosis of cystitis alone having been made.

In the male, confronted with a patient suffering from attacks of cystitis with or without difficulty in urination, with or without distinct diminution in the stream, it is often the practice of the practitioner to introduce a catheter of extremely small size for purposes of irrigation. Strange to say, catheters Nos. 12 to 14 French in caliber are usually resorted to by the inexperienced, in the hope that a small catheter will cause less pain than a large one. It is because of this fact that the presence of *strictures of large caliber* are so frequently overlooked. Such a stricture of large caliber, by virtue of recent inflammatory swelling, may effectually prevent the outflow of urine and cause even retention, while the small catheter will easily enter it, and give no sign of its presence to the introducing hand.

Be, therefore, on your guard, and after preliminary cocainization with 2 per cent. novocain solution in the male, introduce a soft rubber catheter of no smaller size than Nos. 18 or 19 French, and you will be rewarded by finding evidences of urethral coarctation. A most useful catheter in your hands will also be a Mercier or single-elbow catheter of the French silk variety, which should also have no smaller caliber than Nos. 18 or 20 French, lest a narrowing be missed in its passage.

Dilatation with olivary French bougies together with irrigation will bring about an effectual cure.

In the female we occasionally find strictures of the urethra, although they are of considerable rarity as compared with the occurrence of this condition in the male, and the same rule holds good regarding the exploration of the urethra, namely, to use catheters of adequate size.

CONCLUSION

Although we have been unable to give a comprehensive insight into this vast subject, we hope that enough has been said to instil into the practitioner a just appreciation of the significance of the word "cystitis," and express the wish that the medical man in determining his attitude in the treatment of this disease may not think of *cystitis* in the same terms as of local infection—such as felon, appendicitis, or other well localized inflammatory processes—but that he may be aware that cystitis is often but a concomitant and complicating lesion of other diseases, and, that because its forms are so varied in pathology and causation, its prognosis so different, and its response to treatment so capricious, he must invoke a multitude of different diagnostic and therapeutic agents to bring about a satisfactory termination of the disease.

CLINIC OF DR. G. R. PISEK

POSTGRADUATE HOSPITAL

COMMON DISORDERS OF CHILDHOOD

Constipation; Chronic Constipation in Infancy; Treatment in Nurslings; Constipation in the Bottle Fed; Full Discussion of Treatment with Illustrative Cases. Rhinitis, "Coryza"; Treatment. Enuresis; Treatment and Management, Illustrative Cases.

IN our clinical lectures in hospital work we are very apt to lay stress upon those conditions which interest us as clinicians sometimes because of their difficulty in diagnosis, and sometimes because of recently reported advances which tend toward newer lines of treatment. I have been asked to give you a clinical lecture dealing with some of the commoner diseases of early life, to discuss every-day problems which are so apt to be set aside by the lecturer or writer as uninteresting. It is these commonly recurring cases which the practitioner meets daily and that are apt to be treated in a routine, perfunctory manner, that may be of interest, especially when viewed from a different aspect.

CONSTIPATION

This minor malady in early life develops often into the habitual constipation of the adult. Too little attention is paid to this disorder from the standpoint of a real cure. Temporary relief is given and the case dismissed without sufficiently outlining the management so that future recurrences may be controlled.

Atonic conditions of the intestines with deficiency of the muscular wall are complements of general malnutrition brought

about by long improper feeding, or by diseases which themselves are in greater part dependent upon the general nutrition.

At the outset one must recognize that certain congenital anatomic abnormalities may cause habitual constipation which will not be relieved by the ordinary measures. Among these are disproportionate length of the sigmoid flexure, a congenital narrowing of the intestine, and the condition known as Hirschsprung's disease, in which we have a congenitally immense dilatation of the colon. Such anatomic peculiarities will naturally stand in the way of a simple cure, and must be suspected if the usual means fail. An *x*-ray study of the intestinal tract has revealed the presence of many such peculiarities that were formerly unsuspected and which baffled the practitioner in his treatment.

Illustrative Cases.—CASE I.—H. C., eighteen months old, was breast fed for twelve months and has always been a constipated and restless child. Artificial feeding was begun at the seventh month, with modifications of cow's milk. The mother relates that two months ago she noted a lump in the right side of the abdomen of the child, which seemed to disappear. Two or three days ago the lump reappeared, this time in the left side. The next day this mass, which she this time watched closely, appeared much lower in the abdomen. The following day it was in the middle line, where it lodged, and increased in size. The baby then vomited, and cried when his bowels moved and began to show some signs of fever. His physician sent him to us for a diagnosis. Examination disclosed an impacted mass of feces, which was confirmed by rectal examination.

This child was admitted to the hospital, the mass mechanically removed, and the intestinal tract studied. An *x*-ray report showed an enlarged and ptosed colon with thickening of its walls. Dietetic regulation and the free use of mineral oil will be given until the child's condition necessitates operative interference.

CASE II.—M. S., a girl aged eight and a half years, has a history of constipation since early infancy. It was noted that

even as a baby she had an unusually large abdomen. When two and a half years old she had symptoms of "intestinal indigestion," lost weight, and was in very poor condition. At this time the clinical diagnosis of megalocolon was made. When she was four years old she had hemorrhages of the bowels, followed by prolapse of the rectum. At that time the *x*-ray showed an abnormally enlarged colon, which proved to be a typical picture of Hirschsprung's disease.

Her dietetic management has consisted in a marked reduction of the starches and the liberal use of mineral oil daily.

She wears a Van Valzah belt and in the last year has gained 3 inches in height, while previously her growth was constantly subnormal.

Chronic Constipation in Infancy.—When this occurs (which it does not uncommonly) in the breast-fed infant it is also apt to provoke so-called colic, and it may be responsible for stationary weight or even loss of weight or wasting.

In these breast-fed infants examination of the breast milk often shows some peculiarity in the secretion. A low fat content may be the cause, or the total quantity of solids present may be low. In these cases absorption goes on too rapidly and completely, so that little fecal residue is left. The peristaltic movements become sluggish and reabsorption takes place, with the resulting train of symptoms mentioned above.

It is always best to see a sample of the stools on the diaper, as much light may be thrown on the etiologic factors by such an examination. The "dry, putty-like" stools, light colored and friable, occur in those infants in which there is a deficiency in the intestinal secretions. Such findings give a clue to the proper treatment.

In another class of infants the cause is traced to the habitual constipation of the mother; the mother whose weight has increased rapidly after the birth of her child, who now takes little or no exercise, or who is taking a diet to which she has never been accustomed, believing that she is thereby augmenting her milk supply. I refer to the ingestion of large quantities of milk and the consequent lack of desire for other foods, resulting in

constipation. The taking of a great deal of tea and coffee on the part of the mother is another dietetic error which must be sought out and eradicated.

Infants who are mentally deficient, such as cretins, or those suffering from mongolism or from birth injuries producing spastic paralyses, are apt to be habitually constipated. In these children the desire to evacuate the bowel is perverted because of their deficient intellect and imperfectly developed neuromuscular apparatus and control of peristalsis.

The daily use of suppositories and so-called rectal injections almost invariably result in the establishment of an insensitive condition, thus aggravating rather than curing constipation.

Treatment in Nurslings.—The regulation of the mother's dietary is perhaps the most important measure. It is necessary to advise a resumption of a diet that agreed with her before she began nursing her baby—a diet that will contain enough fruit and green vegetables. Further, there must be a regulation of her daily life so that sufficient exercise is taken.

If the fats in the milk are found to be below 2 per cent. these may be increased by eating rare red meats, while the total solids and total amount are often augmented by the ingestion of a generous bowl of yellow cornmeal.

The addition of two or more feedings of a cream-and-water mixture before nursings will increase the supply of fats in cases in which the above measures have failed to produce satisfactory results in the breast secretion. One dram of the top 5 ounces of cream in $\frac{1}{2}$ ounce of water will often supply the fat deficiency, cure the condition, and augment the baby's weight. On the other hand, it must not be forgotten that the giving of fats as a laxative is to be condemned, as it is very often productive of fat, soapy, constipated stools.

The anatomic cases, those with peculiarities of the intestinal tract, as elongated sigmoids, for example, are best treated by the giving of mineral oil daily until regular evacuations are induced. One to four teaspoonfuls daily are necessary in this type of cases. If a fissure of the anus or sphincter spasm are found to be present, these should be removed before any other

treatment is instituted; silver nitrate applications, 15 grains to 1 ounce, followed by salt solution for the fissures and a stretching of the sphincter by the introduction of the little finger of the greased, gloved hand, followed by the fourth and the index-fingers, will readily affect a cure in sphincteric spasm.

The treatment for constipation so often resorted to by mothers, and even nurses and some doctors, must be strongly condemned. I refer to the drastic action of castor oil. Relief is obtained for the time being, but the underlying condition itself is made worse. If drugs are at all necessary they should be mild laxatives, such as milk of magnesia, or the aromatic syrup of rhubarb, or a combination of these in dram doses, best given in the evening.

In cases in which there is a decided deficiency in the intestinal secretions nitrate of potash in 5-grain doses, or the sulphate of soda in 10-grain doses, will stimulate these and obviate the constipation. These drugs are best given in syrup of senna, 15 minims usually being sufficient.

For older infants massage of the bowels, stroking, downward motions over the colon; the use of plain, cool water between nursings, and the early inculcation of stooling on the commode placed in the attendant's lap will produce regularity of the habit and education of the bowels.

Case Reports.—CASE I.—A. P., ten weeks old, has been nursed only to the present, every three hours. He is brought because his desire for nursing has not been as good as usual and because there has been no movement of the bowels without mechanical help. He used to be a good sleeper, but now sleeps little or none in the daytime, and is beginning to be sleepless at night. His weight is 12 pounds, 12 ounces, his birth weight being 8 pounds, 4 ounces. His mother has been making every effort to supply sufficient breast milk, forcing her feedings and taking unusual quantities of milk. She has always been constipated, but is more so at the present time. In this case the mother should take less cow's milk, which evidently constipates her, more green vegetables, particularly those containing "ruffage," and should partake of fruit liberally. The baby will be

given water between feedings, several teaspoonfuls, to which a few drops of orange-juice have been added.

CASE II.—D. H. B., three months old, is nursed every three hours, and has been constipated since birth. Unless there is mechanical help the bowels will not move in forty-eight hours. The stools are yellow, but are hard, dry, and lumpy. The child's appetite is good. The mother confesses to being a tea drinker, taking this beverage in unusual quantities, several cups several times a day.

In this case we have, besides the history of the mother and child, on physical examination, a gas-distended abdomen and a very tight anal sphincter. The stretching of the anus, the dietetic control of the mother, and temporarily the use of $\frac{1}{4}$ grain of phenolphthalein twice a day, given in some breast milk, will correct the condition.

Constipation of the Bottle Fed.—While constipation is perhaps more common in the bottle fed than in the nursling, it is more readily managed, as we have the control of the food in our own hands.

Here one must first eliminate anal fissures or sphincter spasms before undertaking any other form of treatment.

Medicine should have a minor place, in the main relying upon diet, correct habits, and massage. A close study of the formula taken must be made. Boiled milk or milk pasteurized by the flash method are naturally constipating. Formulæ too high in fats will produce lardy, constipated stools. In the anxiety to increase the weight of the child, foods too high in fats are often given, or the fact is overlooked that the milk of cows such as Jerseys has been used, which gives an unusually high fat content. The reduction of the fat to 3 per cent. is often sufficient in these cases to produce a cure.

Proteins should not be materially reduced, as we know how important a factor they are in the nutrition of the infant, having a direct bearing upon the growth of tissue.

The use of sugar in the milk is another important factor toward overcoming constipation. Malt sugar is more apt to

be laxative than any of the other sugars used, and this alone or in combination with oatmeal decoctions very often produces relief, and at the same time has food value. The fruit juices, those of the orange and pineapple, will serve a double purpose, and can be begun early in infancy, even in the third month, if small doses are given at first, well diluted. In the milder degrees of constipation such fruit juices given in teaspoonful doses every twenty minutes to half an hour before feeding morning and evening are often curative.

In marasmic infants 30-drop doses of malt and cod-liver oil preparation not only act as a laxative but also augment the food supply.

Illustrative Cases.—H. J. H., twelve weeks old, weighing 10 pounds, 2 ounces, was brought because he is obstinately constipated and not gaining in weight. He was nursed only for six weeks, the baby refusing to take the breast at that time, and there apparently being very little of the secretion. He was put on barley gruel and Eagle Brand condensed milk, 1 dram to 6 ounces of barley-water, 6 ounces at a feeding, being given every two hours. The child cries a great deal both before and after feeding. We find that he is demanding and taking as much as 54 ounces of this modification a day. That he urinates constantly and freely is not to be wondered at. Here obviously the feeding modification is at fault. A proper modification of cow's milk with maltose sugar, elimination of the constipating barley gruel, and a smaller total quantity of food of a higher caloric value will satisfy this child, and should at the same time correct the constipation and develop his weight and physical condition.

Case II.—E. W., three months old, was nursed to almost three months of age. A week ago he was put upon modified certified milk: 2 ounces milk, 3 ounces water, ½ dram malt sugar; two such bottles to take the place of two nursings. The history is that bowel trouble began seemingly soon after birth. His bowels have always been constipated; they had a greenish cast, and mechanical aid was always necessary to effect a movement. His doctor has been prescribing mineral oil. If the stools

become dry he goes off into a convulsion. This has occurred six times to the present, each one of these convulsions lasting for five minutes. He is weak after these "spells" and refuses his bottle.

On physical examination this child was found to have all the characteristics of mongolism: the typical mongoloid cast of eyes, protruding, irregular shaped ears, flat occiput, and the typical stigmata of his type. The lowered mentality is, in these cases, unresponsive to the ordinary stimulus of the full bowel, and little or no effort is made for expulsion.

Here mechanical aid and the use of mineral oil and massage must be persisted in, at least until the erect position is assumed, when the condition may be to a certain extent obviated.

RHINITIS, "CORYZA"

Another common condition in infants which is productive of a great deal of discomfort and often productive of the most serious consequences is rhinitis, the ordinary "cold in the head." This is due to infection transmitted by direct contact to those in whom the resistance is temporarily lowered by exposure to cold or to prolonged superheated air.

The condition is important in infancy because it produces actual distress, nursing being impeded or rendered extremely difficult in consequence. The tendency is for the spread of the infection to the other mucous membranes, postpharynx, larynx, trachea, and bronchi being successively vulnerable to involvement.

If adenoids are present the rhinitis is apt to be more severe and more apt to cause otitis media. Repeated attacks of "cold in the head" are undoubtedly strong evidence of the presence of adenoid growths; and account for, in some measure, the large number of children in urban populations so affected.

The mother is more apt to regard the condition as worthy of attention than the physician. The routine dose of castor oil is often prescribed over the telephone and the condition allowed to run its course, which it is apt to do in five or six days. This does occur in favorable cases, but to the neglect of these simple colds must be ascribed the many cases of cervical adenitis,

retropharyngeal abscess, otitis, mastoid disease, bronchitis, and bronchopneumonia, which cause the bulk of the morbidity in the early months of life.

Again, the differential diagnosis is important, as many cases diagnosed as simple, subacute, or chronic rhinitis may be found on closer study to have a diphtheric basis. Here the discharge is apt to be more sanguineous than purulent and more profuse in one nostril than in the other.

The rhinitis may be the first noticeable symptom of a congenital syphilitic infection, with the rash and other characteristic symptoms appearing later. That it may be the forerunner of measles must not be forgotten. Koplik's spots and the simultaneous involvement of the larynx and trachea will help in the differentiation.

Treatment.—Relief is often obtained by giving 1 or 2 drams of a laxative, as milk of magnesia, and by the immersion of the child into a tub-bath containing ½ ounce of mustard powder. The installation locally of oils containing drugs will relieve the engorgement of the mucous membranes. Two or 3 drops of liquid albolene, containing ½ grain of camphor and ½ grain of menthol to the ounce, should be instilled after the secretion has been expressed from the nose, the child being held in a recumbent position while the solution is instilled with the medicine-dropper. This should be repeated every hour until relief is obtained, so that the child may be able to nurse or take its bottle properly.

To prevent the danger of infection members of the household or an attendant with rhinitis should be barred from the child's presence. Dusty streets, superheated apartments, ill-ventilated nurseries lend their aid to a lowering of the resistance, and thus to contact infection.

Nasal irrigations or douches are productive of much harm, and should never be used, as they almost invariably carry infection through the eustachian tubes to the middle ear.

Internal medication is rarely needed except for the occasional use of the tincture of belladonna, which may be necessary in aggravated cases which resist local treatment.

ENURESIS

Bed wetting is a fairly common complaint for which we are asked advice, not only from the poor in the dispensary classes but equally from the well-to-do.

The first inquiry should be as to whether the child has at any time been continent, that is, has he overcome the natural or infantile condition of incontinence. The next step is to inquire as to day or night wetting.

There are many causes given as possible etiologic factors in our text-books, and there is no doubt that any of these may be the cause, as, for example, phimosis, hyperacid urine, or adenoids. But, as a matter of fact, these are exceptional causes. The great majority are due to a lack of control of the sphincteric centers or the higher cerebral centers. If voluntary control is obtained or inculcated over the lower centers the case is cured.

Many drugs have been advocated for the relief of this condition, but it is a fact that none of them is specific or nearly specific. Atropin or belladonna has the greatest number of advocates, and there is no doubt that this drug often temporarily assists in the relief, but it does so by decreasing the desire to urinate, thereby lessening the bed-wetting habit.

This habit is more commonly found in active, energetic children, who, by night-time give evidences of neuromuscular fatigue. The cure of this group of cases is dependent upon detailed management, which includes diet, rest, bladder-control exercises, psychic impressions, and in certain intractable cases mechanical irritation of the sphincter.

Having removed any physical causes, such as phimosis, or adenoid vegetations, which latter act through their partial asphyxiation during sleep, the physician must acquaint himself with the details of the child's life, so that fatigue and nerve stimulation may be avoided.

Treatment.—The diet which suits the greatest number of cases includes milk, cereals, bread stuffs, creamed vegetables, eggs and fruits. Meats, meat soups or broth, tea, coffee, pastry, and all highly seasoned foods or entrées are excluded.

A two-day rest cure is given, requiring that the child have

his breakfast in bed, and is not allowed out of bed until lunch time. Such a plan is followed for two days each week, at the beginning and end of the week.

A "dry supper" is given in the evening, that is, no milk or any liquid is allowed after 4 P. M.

The child is allowed no romping or strenuous play and no excitement.

The child is put to bed an hour after his supper and taken up to urinate when the parents retire at 10.30 P. M. or thereabouts.

During the day the child is required to urinate and to stop urinating at the word of command. This fixes the attention of the higher senses on those of the lower, and to my mind this is a very important factor in the management and control of the condition. The control exercises are done at least three times a day in the presence of an attendant.

The patient is given a report card which he or she should fill out every morning, indicating whether the bed was wet or dry, and the number of times the control exercises were done.

Sample report card:

Date..... Name.....

Bed wet..... Bed dry.....

Number of times control exercises done.....

Illustrative Cases.—N. S. C., $3\frac{3}{4}$ years old, referred to us by her physician, who states that she has always wet the bed and also is incontinent in the daytime. She never has a dry night. They have tried all the usual remedies without success. Otherwise she is considered a well, normal child. With the exception of a slight knock-knee this latter observation was confirmed. The child, who was of good mentality, apparently had never gained control over the bladder. The plan outlined above was applied. In her case no drugs were given. At the end of the first eleven days she had earned but one golden star. Out of the next three weeks she was dry 50 per cent. of the time. In the

subsequent weeks only occasionally did she wet the bed or her clothes. In three months she was entirely relieved of her incontinence.

CASE II.—T. S., eight years, eleven months old, had pneumonia two years ago following an attack of measles. Since that time she has lost her urinary control at night. She had symptoms of chorea a year and a half ago. She attends school and is bright, but irritable. Otherwise she is considered well and strong. Physical examination showed no local cause for her disorder, but because of her history she was put upon atropin, grain $\frac{1}{350}$, and tincture of hyoscyamus, 4 drops at bedtime. The control exercises and diet were ordered as outlined above. Her record shows that she did her control exercises at least twice a day and often five times in the day. The first week after her visit she wet the bed but once, and once a week for the next three weeks, after which time she became entirely continent. Medication was early discontinued, but the control exercises were persisted in for some weeks.

Young children who have not yet learned to write may affix gold stars for a dry bed and red stars for a wet bed. These reports which the child mails to the physician make a deep impression and are extremely valuable adjuncts in the cure. Fluids are allowed in the diet as rewards only after the child has demonstrated the power of control and has once more become continent.

CLINIC OF DR. HERMAN O. MOSENTHAL

VANDERBILT CLINIC OF COLUMBIA UNIVERSITY

THE SYMPTOMS AND TREATMENT OF RETENTION OF WASTE PRODUCTS IN NEPHRITIS

A Case Exhibiting Albuminuria of Six Years' Duration. The Problem of Treating this Conditon. Every Nephritic Patient Does Not Suffer from a Retention of Excretory Products, and a Careful Physical Examination, as Well as Thorough Laboratory Tests, is Necessary to Determine the Substances which are Not Adequately Eliminated. A Discussion of the Significance of the Symptoms and Functional Tests in Nephritis in Their Relation to the Retention of Urinary Excretory Products and to Treatment.

THE patient before us this morning is a girl of eighteen, a stenographer, an American. She tells us that six or seven years ago she had a febrile disease, diagnosed as pleurisy; no sputum was examined and she does not remember that she ever had a persistent cough; she was in bed three weeks at that time; during her convalescence a slight trace of albumin was found in the urine; this has persisted. Five months ago the albuminuria became much more marked and swelling of the ankles and legs developed; lately there has been puffiness of the face in the morning and the size of the legs has increased toward evening. She has no headache, no visual disturbance, or any other complaint.

She had typhoid fever eight years ago; in childhood there were frequent attacks of tonsillitis, which ceased after tonsillectomy. The history is negative in all other respects.

Physical examination shows a tendency to obesity; height 5 feet, 2½ inches, weight 143 pounds. When she was first seen the edema, which you may judge still persists by the puffiness

about the eyes and the rather deep pitting above the ankles, was more marked and the weight was correspondingly greater. Probably she is now carrying about 5 pounds of fluid as subcutaneous edema. Even allowing for this, she is still a little over weight. A careful examination of the heart, lungs and abdomen, and extremities revealed no abnormalities. The blood-pressure is 135/75. There is a slight secondary anemia. Hb. 68 per cent., R. B. C. 4,568,000.

The urine on test-meal was as follows:

Time of day.	C.c.	Specific gravity.
8–10	505	1.012
10–12	210	1.014
12– 4	235	1.007
4– 6	153	1.011
6– 8	165	1.011
Total, day	1268	
Night, 8–8	884	1.012
Total, twenty-four hours	2152	

The albumin content varied from 3 to 7 grams per liter in various specimens. There was as intense an albuminuria in the erect as in the prone position. The microscope revealed very many leukocytes, a few red blood-cells, and a few leukocyte casts. The phthalein excretion was 51 per cent. in two hours and ten minutes. The blood urea nitrogen 16.7 mg. and the creatinin 1 mg. per 100 c.c. The noteworthy features here are the albuminuria, hematuria, leukocyte casts, and edema, with negative findings in every other respect. The phthalein is slightly diminished and the blood urea nitrogen a trifle increased, indicating a minimal retention of urinary excretory products. The test-meal for renal function is of rather low specific gravity and the volume is somewhat increased; these changes are in large part due to the fact that this patient is eliminating her edema and is a valuable indication of this fact. Such cases presenting albuminuria and edema without increased blood-pressure have been variously called parenchymatous nephritis and nephrosis. The latter term is supposed to indicate that the principal lesion is a degenerative and not an inflammatory process, and is largely

confined to the tubules. The presence of a large number of leukocytes, a few red blood-cells, and leukocyte casts in the urine tells us that an inflammatory process exists in these kidneys. It is probable that this patient is suffering from an acute exacerbation of a chronic condition. The increase in the albuminuria and onset of edema five weeks ago are the basis for this assumption.

There is a tendency to treat all cases of nephritis according to a system by which the kidney is spared as much as possible. The food intake and physical and mental exertions are restricted within very narrow limits. This method plays safe as far as the kidneys are concerned, but insufficient food and inadequate physical and mental exercise may incapacitate the remainder of the body and render the patient more of an invalid than before the physician exercised his authority. It is obvious that in our patient, for instance, there is a considerable retention of water, but only a very slightly deficient excretion of the other urinary excretory products. The problem arises how the albuminuria, the blood-pressure, etc., are to be interpreted in relation to the therapy that is to be directed in two directions: first, to restore the kidneys to normal as far as possible, and second, to maintain the nutrition and efficiency of the patient. A third factor, that of toxemia, is present in some cases of nephritis. This is independent, in many instances, of renal insufficiency. Such patients may exhibit typical uremic convulsions while their blood urea is at a normal level and the kidney action apparently adequate. In our case this condition does not pertain.

The functional kidney tests and various symptoms of nephritis indicate how far the efficiency of the kidney has been impaired, and to what degree retention of urinary products within the body has progressed. The interpretation of the significance of such findings is, unfortunately, largely a matter of personal impressions and experiences. It is not possible at the present moment to put them in logical sequence without producing a false sense of security, because any such arrangement would be forced and not agree with the known facts. Hence, a few of the more important points are chosen for discussion, and no attempt

is made to formulate a picture that would represent the progress of nephritis and give the indications for treatment at each step.

Albuminuria.—In 1901 Sir William Osler[1] wrote a short article, much quoted since that time, "On the Advantages of a Trace of Albumin and a Few Tube-casts in the Urine of Certain Men Above Fifty Years of Age." He called attention to the fact that the urinary findings were of less importance in determining the character of the disease than some other signs. In other words, many cases of albuminuria, even those that are fifty years old and whose urine contains not only a trace of albumin but a great deal of albumin, are not necessarily in danger of their lives because of renal insufficiency, and they should not be treated for such a condition if it does not exist, as has so frequently been done.

Granted that an albuminuria originates from the kidney and is caused by Bright's disease, it becomes the physician's duty first to ferret out the cause of the nephritis and eradicate it; if this be not possible, the next step is to attempt to reduce the albuminuria by the usual therapeutic measures of a bland diet and rest in bed. Irritating as it is to our desire to achieve ideal results, it must be confessed that in some patients the albuminuria cannot be controlled. The main point it is intended to emphasize at the present time is that with the newer methods of blood and urine examinations (to be alluded to subsequently) it has come to be appreciated that many cases with marked albuminura have no signs or symptoms of retention due to deficient kidney action. It may thus be frequently demonstrated that the end-products of protein metabolism are eliminated without difficulty and that our former empiric fear of protein food has no foundation.

Epstein,[2] indorsed by Sir T. Clifford Allbutt[3] and John R. Williams,[4] has been most enthusiastic about feeding cases with marked albuminuria and edema a rather high protein diet, be-

[1] Osler, W., New York Med. Jour., 1901, lxiv, 949.

[2] Epstein, A. A., Jour. Amer. Med. Assoc., 1917, lxix, 414; Amer. Jour. Med. Sci., 1917, cliv, 638.

[3] Allbutt, T. C., Brit. Med. Jour., 1918, ii, 395.

[4] Williams, John R., State Jour. of Med., 1919, xix, 12.

lieving that among other good effects the nutrition of the patient may be improved by this means. If the blood urea or non-protein nitrogen are high, this form of dietetic therapy is contraindicated. Whatever may be said in regard to the effect of protein food on the edema, if it be present, it must be acknowledged that it is borne well, that no uremia develops, and that bodily efficiency may be maintained thereby.

My own[1] observations lead me to believe that a full diet is the best means we have to rectify an anemia. Iron without a proper diet has proved itself to be useless in most instances, especially in nephritis. It is very desirable for the nephritic to have a normal number of red blood-cells, not only to maintain his efficiency but also to furnish a proper stimulus for kidney action, inasmuch as the urine becomes less concentrated and retention of renal excretory products is favored when anemia exists.[2, 3, 4]

It is very gratifying to know that some of these cases of chronic diffuse nephritis may have a persistent albuminuria for years without progressive encroachment upon the kidney functions. Thus a woman of forty years of age who has had a marked albuminuria for fourteen years shows a phenolsulphonephthalein excretion but little below normal (45 per cent. in two hours) and a non-protein nitrogen of 30, a urea nitrogen of 14.6, and a creatinin value of 1 mg. per 100 c.c. of blood, all of which may be considered within the upper limit of normal; the variation of the specific gravity in the two hourly specimens of the renal test-meal are also normal. Her general condition is good as far as the effects of her albuminuria are concerned; she has no secondary anemia. A somewhat similar case is that of a young electric engineer who has always worked hard. Seven years before his present examination he had an acute nephritis, followed by a marked and persistent albuminuria. His tests for renal function have always been normal and do not show any decrease

[1] Mosenthal, H. O., Bull. Johns Hopkins Hosp., 1918, xxix, 129.

[2] Ibid., Arch. Int. Med., 1915, xvi, 733.

[3] Mosenthal, H. O., and Lewis, D. S., Jour. Amer. Med. Assoc., 1916, lxvii, 933.

[4] Christian, H. A., Arch. Int. Med., 1916, xviii, 429.

during six years. His diet has contained sufficient calories and protein to maintain him in good health.

The conclusion to be drawn from it all is that if an albuminuria cannot be cured, it in itself is not an indication that the patient is to be restricted to the life of an invalid, but that it is wise to disregard the albuminuria and treat the case according to the physical signs and newer laboratory tests that indicate what may be expected from the heart, arteries, and kidneys. This does not mean that all precautions are to be thrown to the winds, nor that every case shall be safeguarded by limitless routine restrictions, but that if the indications we now have at our command warrant it, the patient's diet, exercise, and occupation should be so regulated that while physical and mental fitness are maintained, there will be no overstrain of any of the bodily functions.

Hypertension.—Increased arterial hypertension was formerly regarded as a signal that a marked degree of contracted kidney existed. Thanks to the efforts of many men, initiated by Sir T. Clifford Allbutt, it is now generally acknowledged that hypertension may exist as an independent disease, variously known as hyperpiesis (Allbutt), primary hypertensive cardiovascular disease (Janeway), or essential hypertension. The point which it is desired to emphasize is that arterial hypertension cannot be intelligently treated until a thorough investigation of renal function has been made. There is no clinician so astute as to recognize whether or not retention of renal excretory products exists without the aid of laboratory procedures. The treatment of hypertension, in every instance, involves at least two factors: First, the care which the patient must take of himself in order to forestall the effects of the strain to which his heart and arteries may be subjected; and, second, the measures which are designed to make life possible if a certain degree of renal impairment be found. The retention of urinary products may be handled in most individuals as though hypertension did not exist. There is a wide-spread impression abroad that protein, especially animal protein, in the food aggravates the blood-pressure. Some very keen and careful physicians tell me they have substantiated

this. In my hands some very accurate observations have failed to convince me that this is true in all cases. When renal tests permit it the feeding of hypertensive patients should be so regulated that full nutrition is maintained, but that obesity is avoided. To accomplish this end meats, either red or white, are invaluable; in most instances they produce no ill-effects, though this is probably a matter to be studied individually in each patient.

TESTS FOR RENAL FUNCTION AS A GUIDE TO THE TREATMENT OF RENAL INSUFFICIENCY

Under this heading it is desired to discuss the various functional tests now in vogue, and to make an attempt to formulate what therapeutic indications each one of these furnishes. The following tests will be taken up:

1. Diminished power of the kidney to concentrate the urine.
2. The non-protein nitrogen, urea, creatinin, and uric acid in the blood.
3. Ambard's constant.
4. Phenolsulphonephthalein test.

Retention due to insufficient kidney action is often taken for granted as being present in every case of nephritis. That this is not necessarily so has been mentioned under the headings of Albuminuria and Hypertension. Before a patient is plunged into the rigorous restrictions of curtailing his food, diversions, and occupation to the limit, it is well to get a survey of the indications for treatment which various functional tests may furnish. The present considerations take up the subacute or chronic conditions and not the acute. In the last very stringent restrictions may be applied with great benefit over short periods; in the former, however, such radical limitations may treat the disease but not the patient.

Diminished Power of the Kidney to Concentrate the Urine.—The ability of the kidney to eliminate any solid substance depends upon two distinct factors: First, the power to concentrate the given material in the urine; and, second, the amount of water that can be excreted. In interpreting functional tests this fundamental principle is frequently disregarded, and yet it

is of very great importance if a proper use is to be made of the data obtained. It is rather usual to speak of a normal phthalein excretion or of a low blood urea as being satisfactory without inquiring into the mode in which the substances have been eliminated at a rapid rate. If large amounts of urine are necessary to carry them away, then one of the factors of safety, that of concentration, has been lost. By means of testing the amount of urine voided at night and observing closely the specific gravity of the urine, the desired information on these points may be obtained.

Nocturnal Polyuria.—One of the first manifestations of renal insufficiency is often found in nocturnal polyuria. If an individual takes no food or fluid after the evening meal and collects the urine for a period beginning three hours after that and ending at breakfast the next morning, that is, for about ten hours, the normal quantity of urine voided is usually 400 c.c. or less,[1] though it may be as high as 750 c.c.[2] An amount in excess of the latter value is decidedly high, and a cause must be sought for it. This may be found in diseases that must not be confounded with nephritis, such as cystitis, pyelitis, anemia, hypertrophied prostate, polycystic kidney, elimination of edema, diabetes, or diabetes insipidus. The reason for nocturnal polyuria in subacute or chronic nephritis is an inability of the kidney to eliminate sufficient solids during the daytime so as to make the night a period of comparative rest and inactivity. This is equivalent to saying that there is a lag in urinary secretion. The excess of water voided at night is present not only because there is a residue of solid material to be excreted but also because the power to concentrate the urine at higher levels has been lost. In other words, such persons are taking an amount of food which their kidneys must excrete by an abnormal degree of effort. By changing the diet to one of a lower level of protein (for it is the end-products of protein, as well as the water and salts that are excreted in the urine, whereas the substances resulting from the digestion of carbohydrates and fats are

[1] Mosenthal, H. O., Arch. Int. Med., 1915, xvi, 733.
[2] Ibid., 1918, xxii, 770.

excreted through other channels) the nocturnal polyuria is often set aside.

Thus in a series of 21 patients exhibiting nocturnal polyuria on either a low or a moderately high protein diet there were 19 whose high night urine occurred only in the specimen corresponding to the high diet, and but 2 in whom the opposite held true. In every instance, however, the amount of salt and nitrogen eliminated was greater with the larger quantity of night urine, indicating that in the two exceptions noted other influences than diet had to be considered. It may be concluded from these data that nocturnal polyuria is a compensatory phenomenon which effects the elimination of retained urinary excretory materials, and that such a strain upon the kidney may be set aside in most instances by a suitable diet.

Polyuria has generally been accepted as a most fortunate compensatory phenomenon, which aids the nephritic in getting rid of waste products. This is undoubtedly true. Foster[1] has shown how an increased amount of nitrogen may be eliminated in this way. It is well known that, especially in diabetes insipidus, huge amounts of fluid may be excreted over long periods and the kidney apparently suffer no harm. In nephritis, however, as Schlayer originally stated, the kidney may become fatigued when overstimulated and, instead of showing an increased response, answer by diminished elimination. This is certainly true in some instances. I have seen it occur after glucose infusions, after the intake of inordinately large amounts of fluid, and when water was forced over several weeks, finally resulting in a gradual diminution of the urinary flow and death from uremic coma. For these reasons it is advisable not to overburden the kidney and to prevent polyuria and nocturnal polyuria if possible by a suitable diet.

There is one factor in the management of these problems which is often lost sight of. The minimal amount of protein which the body metabolizes is not that occurring during starvation, but on a high carbohydrate diet. An individual will eliminate about 8 grams of nitrogen per day in his urine during starva-

[1] Foster, N. B., Amer. Jour. Med. Sci., 1916, cli, 49.

tion; if a high carbohydrate diet be given this may be cut down to 4 or 5 grams. Therefore, a diet with about 5 to 6 grams of nitrogen (35 to 40 grams of protein) a day would be ample to maintain nutrition and would spare the kidney very much. Such a low protein, high carbohydrate diet is one that offers the best means of feeding when nitrogen retention has to be dealt with in nephritis.

Low Fixed Specific Gravity of the Urine.—Another sign of renal insufficiency which occurs very early in nephritis is a low fixed specific gravity of the urine in the neighborhood of 1010. Osler, in the article previously mentioned, called attention to the serious significance that this phenomenon of inability to concentrate may have. It is possible to learn a great deal from the specific gravity even of single specimens; it is well established that a specific gravity of 1020 or more signifies that the kidney possesses a power of concentration which is sufficiently high to be classed as normal; any impairment of renal function, if it exists, must under those circumstances be sought in a diminished output of urinary volume. Such conditions are most frequent in myocardial insufficiency, that is, passive congestion of the kidney, and in many cases of acute nephritis.

Single specimens with a low specific gravity, even if they occur repeatedly, cannot be accepted as final evidence of a loss of power of concentration. Thus in a patient with marked albuminuria and hypertension the following twenty-four-hour samples were collected and the specific gravity noted:

Date.	Specific gravity.
May 2	1011
May 3	1012
May 7	1010
May 8	1009
May 9	1010
May 10	1010
May 16	1010

However, when the urine was collected at two-hour intervals, and food and fluid were only given at meal-times, a different picture developed:

Time.	Vol.—c.c.	Specific gravity.
6– 8 A. M.	205	1016
8–10 A. M.	123	1010
10–12 P. M.	275	1012
12– 4 P. M.	500	1011
4– 6 P. M.	425	1001
6– 8 P. M.	230	1009
8–10 P. M.	122	1020
10 P. M.–8 A. M.	230	1020

The height to which the specific gravity rises (1020) is satisfactory, and the variation from the highest to the lowest indicates a very great flexibility of the kidney to accommodate itself to the demands made upon it. A more detailed study in this patient than the observation of individual specimens was, therefore, necessary to determine the true state of renal function. The other tests bore out the fact that in this case the power of the kidney was not impaired.

The statements made under nocturnal polyuria in regard to kidney fatigue, etc., apply here as well, and need not be repeated. It should be emphasized, however, that if a low fixed specific gravity of the urine exists, even though other tests for renal function indicate normality, that one distinct element of kidney efficiency, that of concentration, has been diminished. The apparently unimpaired eliminative action of the kidney is brought about by a compensatory polyuria. Such cases often do well for a long period, and are, to all appearances, in very good health, but if their urine volume diminishes they are in grave danger of suffering severely from retention. They should, therefore, be observed most carefully and every possible effort should be made to shield them from overstrain, according to the principles already laid down under nocturnal polyuria, and to treat any tendency to oliguria with due attention.

The Non-protein Nitrogen, Urea, Creatinin, and Uric Acid in the Blood.—The older, cumbersome method of balancing the output and intake of various materials in order to estimate the kidney's ability to eliminate any given substance has been largely discarded; not only is it difficult to carry out, but it may lead to false conclusions as the nitrogenous substances may be assim-

ilated and not retained because of insufficient excretion.[1] The various quantitative blood-tests, on the other hand, are a perfectly definite measure of the difference between the end-products of nitrogen metabolism and the quantity eliminated in the urine. Of the substances under discussion, largely for technical reasons, the blood urea and creatinin have found most favor, the non-protein nitrogen and uric acid being resorted to less frequently.

The upper normal values are non-protein nitrogen 30 mg., urea nitrogen 15 mg., uric acid 2 mg., and creatinin 2 mg. per 100 c.c. of blood.[2] It is very interesting to note that these products are retained in definite order as the permeability of the kidney is lowered; the first to increase in the blood is uric acid, the next urea, and finally creatinin.[3] The value of these observations is much enhanced by their confirmation and elaboration. Myers and Killian in their last article on the subject note that creatinin increased in the blood only after considerable retention of urea had taken place and the nephritis was rather far advanced; that cases with 5 mg. of creatinin or more almost invariably have a bad prognosis, although such patients may be up and about and in exceptional instances live for one year.[4] Recently it has been demonstrated that the uric acid concentration of the blood is the most delicate test of renal function at our disposal.[5] It reveals an impairment of kidney activity even before the test-meal procedure, which hitherto has been regarded as the most sensitive indication of renal activity at our command.[6]

It is appreciated that an accumulation of non-protein nitrogenous substances may occur in the blood because of increased protein destruction, desiccation of the individual, or impairment of renal function.[7] In its final analysis the phenomenon is one

[1] Mosenthal, H. O., and Richards, A., Arch. Int. Med., 1916, xvii, 329.

[2] Myers, V. C., and Lough, W. G., Arch. Int. Med., 1915, xvi, 536.

[3] Myers, V. C., Fine, M. S., and Lough, W. G., Arch. Int. Med., 1916, xvii, 570.

[4] Myers, V. C., and Killian, J. A., Amer. Jour. Med. Sci., 1919, clvii, 674.

[5] Baumann, L., Hausmann, G. H., Davis, A. C., and Stevens, F. A., Arch. Int. Med., 1919, xxiv, 70.

[6] Mosenthal, H. O., and Lewis, D. S., Jour. Amer. Med. Assoc., 1916, lxvii, 933.

[7] Mosenthal, H. O., Arch. Int. Med., 1914, xiv, 844.

of retention, and if the kidney were performing its function perfectly there would be sufficient elimination to maintain a normal composition of the blood no matter what the contributing factors of protein destruction, desiccation, etc., might be. Our conception of what influence these retained substances have upon the patient have changed a great deal since the time when uremia received its name. Today some doubt exists whether urea in itself is at all toxic. The ingestion of large amounts of urea forcing the blood urea up (as high as 111.4 mg. of urea nitrogen per 100 c.c.) produces a certain train of symptoms comparable to those encountered in the asthenic type of uremia: headache, dizziness, apathy, drowsiness, bodily weakness, and fatigue.[1] Such symptoms appeared when the blood urea nitrogen rose above 68.2 per 100 c.c. and disappeared when it fell below this level. These observations would indicate that certain toxic phenomena could be ascribed to an accumulation of urea in the blood. On the other hand, there have been patients, as seen by most physicians interested in this condition, who have had greater amounts of blood urea nitrogen over long periods without exhibiting any of these symptoms. That uremia, particularly of the so-called sthenic type, may exist without an increase of nitrogenous excretory products in the blood and tissues is now thoroughly appreciated. The increase of blood urea and of creatinin in the blood therefore signify especially insufficient kidney action; they foretell that the patient is in serious danger when the blood urea nitrogen reaches a level of 65 and the creatinin one of 5 mg. per 100 c.c.

It is certain that symptoms frequently appear when retention of the end-products are marked. The experiments of Hewlett and his colleagues would indicate that urea is one of the substances responsible; Meyers and Killian believe that the creatinin is a factor; whatever the toxic materials are, whether one or more, nitrogenous or non-nitrogenous, it is well established that they produce their effect when nitrogenous waste material is retained in the blood. From the therapeutic point of view it

[1] Hewlett, A. W., Gilbert, G. O., and Wickett, A. D., Arch. Int. Med., 1916, xviii, 636.

is, therefore, indicated to keep the blood free from the accumulation of such substances, thus producing a margin of safety, and, furthermore, to remove the excessive stimulus and irritation to the kidney and the possibility of developing renal fatigue (as discussed under Nocturnal Polyuria) with its consequent diminished urinary secretion, entailing a retention of deleterious substances within the body. Frothingham and Smillie[1] were among the first to show how the non-protein nitrogen could be diminished in the blood by a low protein diet. The same principles of sparing nitrogen by means of raising the carbohydrates in the food may be applied here as detailed under Polyuria. In some instances the diet, however high it be in carbohydrates and low it be in proteins, will not serve to reduce the retention products within the blood to normal. Evidently in such individuals the kidney threshold to these substances is materially raised. These cases offer a very poor prognosis. One patient in whom the non-protein nitrogen of the blood was reduced from 145 to 32 mg. per 100 c.c. and the urea correspondingly, invariably exhibited uremic symptoms when enough protein was given to maintain his nutrition.

The following diet has been found to be of value in these severe cases or whenever it is intended to reduce the retained waste products as quickly as possible. It has the advantage of not requiring to be weighed, inasmuch as, even when the patient eats whatever he may desire of these articles of food, he will not consume more protein than is required to cover the minimum he would excrete on a high carbohydrate diet. Alcohol, which may or may not be allowed, I have not found to be an irritant to the kidneys in small quantities.

LOW PROTEIN HIGH CARBOHYDRATE DIET

(Salt, sugar, and butter may be used as desired, and need not be weighed or measured.)

Breakfast:

Sherry, 30 c.c.
Baked apple, stewed prunes, orange
"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch).
Cream, 15 c.c.

[1] Frothingham, C., and Smillie, W. G., Arch. Int. Med., 1915, xv, 204.

Dinner:

Sherry, 30 c.c.
Potato, baked or mashed.
String beans, cabbage, carrots, lettuce, onions, tomatoes, cucumber pickles.
Fruit cornstarch pudding, fruit tapioca pudding.

Supper:

Same as dinner.

NITROGEN CONTENT OF FOODS USED IN LOW PROTEIN DIET

Article of food.	Percentage of nitrogen.
Cream	0.41
Cereal:	
"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch)	0.13
Fruit:	
Baked apple	0.04
Orange	0.16
Stewed prunes	0.14
Vegetables:	
Cabbage	0.16
Carrots	0.10
Lettuce	0.24
Onions	0.17
Cucumber pickle	0.10
Baked potato	0.48
Mashed potato	0.40
String beans	0.23
Tomatoes	0.23
Desserts:	
Blackberry cornstarch pudding	0.05
Prune cornstarch pudding	0.07
Apple tapioca pudding	0.02
Peach tapioca pudding	0.06

This diet is preferable to the milk diet or Karell diet to meet the nitrogen retention, inasmuch as by its high carbohydrate content it necessitates less protein destruction, and consequently calls for a smaller amount of nitrogen to be excreted.

When the waste products in the blood have been reduced to

normal, or earlier in mild cases, protein should be added to the food so that at least 40 to 60 gm. of protein per day are taken. The quality of the food and its amount must be largely regulated according to the individual's needs and tastes, and definite diets that can be used in every instance are not at hand.

The means of managing these conditions outlined thus far concern themselves with only one phase of the question, namely, that of regulating the intake so as to place it in proper balance with the excretory power of the kidney. This undoubtedly is the safest mode of procedure which offers itself. When recourse must be had to other measures there is a distinct loss in the margin of safety. The increased water ingestion suggested by Foster has already been mentioned. As a matter of fact, most of these patients drink the optimal amount of water for them without any urging. It is remarkable how frequently they volunteer the information that they are relieved of an incessant desire to drink water when they are placed upon a low protein, high carbohydrate diet. Unsually when any but dietetic measures are necessary to control accumulated nitrogenous waste products, we are confronted with the problem of treating actual or threatened uremia, and the means of solving it may be deferred until that section is taken up.

That proper hygienic management and regulation of the life of these cases go hand in hand with the above treatment is self-evident. However, the indications for such therapy is to be found in the state of the heart and blood-vessels, the presence or absence of complications, and the subjective symptoms. They need not, therefore, be considered as being associated with retention of non-protein nitrogen.

Ambard's Constant.—By determining the proportion of the urea in the blood to that excreted in the urine according to Ambard's laws and the formula derived therefrom, an idea as to the power of the body to excrete urea can be obtained.[1] As the urea in the blood increases, it exercises a correspondingly greater diuretic stimulus, and the urinary urea rises proportionately. In other words, in any given individual Ambard's

[1] Lewis, D. S., Arch. Int. Med., 1917, xix, 1.

constant does not change even though the blood urea fluctuates very markedly. This furnishes us with a means of determining very accurately the degree of renal function present, and should not be confounded with the information derived from the blood urea, which involves other factors and must be looked upon as the resultant of dietetic regulation on the one hand and renal function on the other. The blood urea necessarily fluctuates widely. Ambard's constant, however, remains fixed unless the disease process changes and renal function either improves or deteriorates.

Whereas the blood urea and creatinin can largely be employed as indications for dietetic therapy, Ambard's constant has its greatest usefulness in furnishing information in regard to the progress of nephritis as measured by frequently repeated tests and indicating renal function when the blood urea may be low as the result of dietetic therapy. According to Ambard's formula 0.09 or less indicates normality, 0.351 or over is a sign of impending danger.[1] McLean has changed the mode of figuring the constant somewhat, having his normal figures at 80 or higher, and a change for the worse being indicated by a lowering of the constant. This method of calculation is often spoken of as McLean's index.[2]

The **phthalein test** (or the "red test" as it is called) is so well known and so generally used that even a short description of it is out of place. It is invaluable as a general indication of progress in nephritis, and if frequently repeated reveals the course of the disease, as affected by therapeutic measures, in a very satisfactory manner. It does not furnish a spcific means of testing out the immediate success of therapy aimed at removing products which have been retained, and it is not possible to use it as a guide for treatment in the sense that polyuria, lack of urinary concentration, and the increase of non-protein nitrogenous constituents of the blood can be employed. However, its prognostic value both for the immediate outlook and, in frequently

[1] Mosenthal, H. O., and Lewis, D. S., Jour. Amer. Med. Assoc., 1916, lxvii, 933.

[2] McLean, F. C., Jour. Exper. Med., 1915, xxii, 212.

repeated observations, for the inroads the lesion of the kidney is making upon renal function, is of very great value in directing the intelligent supervision of chronic nephritis.

CLINICAL CONDITIONS INDICATIVE OF RETENTION OF URINARY EXCRETORY PRODUCTS IN NEPHRITIS

There are certain syndromes included under this head that merit individual consideration because the therapeutic procedures which they call for are almost specific. Those which it is intended to discuss are:

1. Edema.
2. Uremia.
3. Acidosis.

Edema in the present discussion may be looked upon as a symptom of fluid retention. Care must be taken in examining the patient so as to be certain that myocardial insufficiency does not play a part in its production. The best results in treating this feature of retention in nephritis have been obtained in recognizing the fact that the inability to excrete water on the part of the kidney is closely associated with that of salt elimination. Whether the body tissues or the kidney is at fault, and whether water or sodium chlorid is the primary substance that is retained, is a speculative matter that admits of argument on either side and is very far from being solved.

A salt-free diet, including in obstinate cases salt-free bread, butter, etc., will in almost every case yield gratifying results. With some patients it requires three or four months of faithful insistence on the diet, but success usually crowns the effort. It is a very strange phenomenon to note how suddenly the oliguria gives way to polyuria, and salt retention to free elimination. The rapidity of the transformation points to a change in some of the chemical reactions within the body rather than to a healing process in a kidney lesion, which must, of necessity, be of gradual development. A case in point is the following, which happened to be undergoing routine of a test-meal for renal function on the day upon which the edema first showed a tendency to be eliminated; the development of polyuria after the preced-

ing low fluid excretion is very decided, the change from a high to a low specific gravity and the increased elimination of salt without a corresponding increment in the nitrogen are very evident and interesting.

Time of day.	C.c.	Specific gravity.	Sodium chlorid.		Nitrogen.	
			Per cent.	Grams.	Per cent.	Grams.
8–10	40	1.021				
10–12	63	1.021				
12– 2	35	1.020				
2– 4	57	1.018				
4– 6	83	1.017				
6– 8	228	1.009				
Total, day	506	.....	0.57	2.88	0.66	3.34
Night, 8–8	1228	1.010	0.50	6.14	0.33	4.05
Total, twenty-four hours	1734	.....	....	9.02	....	7.39
Intake	1760	.....	....	3.00	....	13.40
Balance	26			6.02		6.01

Edema or anasarca in itself does not produce any harmful effects unless the fluid accumulations in the pleura, peritoneum, pericardium, and beneath the skin become so great as to interfere mechanically with the circulation and other vital functions. Under these circumstances it is necessary to relieve the situation by mechanical removal of some of the fluid. Tapping the chest, I believe, furnishes the readiest means to accomplish this; it may be frequently repeated and apparently does not have any drawbacks associated with it. In some instances, though they are extremely rare, the withdrawal of ascitic fluid may be indicated; this is followed by more discomfort and prostration, and peritonitis occasionally ensues. Enormous amounts of fluid may be drained away through Southey's tubes or skin incision. If either of these methods are resorted to the danger of possible infection must be borne in mind and guarded against.

Purging and sweating, as accessory dehydrating measures, are often useful. In every case the bowels should be kept well open. Hot packs and similar measures have in my hands not yielded results which could not be obtained by less debilitating

means. The use of diuretics always holds out a temptation as a simple solution of the problem. When the heart is insufficient, digitalis, especially when combined with theocin or other drug of the caffein group, acts almost like a specific. When it is a question of stimulating the kidneys directly the problem is an entirely different one. With an exhibition of such drugs an oliguria instead of a polyuria often ensues. In carefully regulated animal experiments the effects of diuretics may be foretold definitely[1]; in patients this cannot be done. Occasionally a small dose of caffein may be followed by good results.[2] However, it is best to avoid the use of diuretics, unless they are employed very carefully, starting with small doses, never using them continuously, but intermittently, and always noting what effect they have upon the urine volume, so that they may be discontinued in case oliguria instead of polyuria is produced.[3]

Epstein[4] has lately formulated a theory concerning edema in which he maintains that the lack of proteins in the blood is responsible for a diminished osmotic pressure, thus allowing the water to pass through the blood-vessels into the tissues. The treatment aimed at remedying this pathologic state consists in a diet of from 80 to 200 gm. of protein, with a small quantity of carbohydrate and a total restriction of fats. In other words, a high protein diet, whose aim is to restore the impoverished blood to normal, is advocated. Sir T. C. Allbutt[5] has endorsed this treatment. It is, of course, contraindicated if the elimination of nitrogen is deficient as indicated by a rise in the blood urea. Whether or not this form of therapy will prove to be of value still remains to be determined. In employing it, one indication, that of nourishing the patient more successfully than has been done hitherto, is fulfilled. The importance of this has already

[1] Mosenthal, H. O., and Schlayer, C., Deutsch. Arch. f. klin. Med., 1913, cxl, 217.

[2] Janeway, T. C., Trans. of the Congress of Amer. Phys. and Surg., 1913, ix, 14.

[3] Christian, H. A., Amer. Jour. Med. Sci., 1916, cli, 625; Arch. Int. Med., 1916, xviii, 606.

[4] Epstein, loc. cit.

[5] Allbutt, T. C., loc. cit.

been discussed under Albuminuria. Some patients lose their edema promptly when a high protein diet is given, others do not; such a diet, of course, may be made salt poor, and part of its success may be atrributed to that element; in other cases this scheme does not meet with success.

After the edema has cleared up it becomes necessary to adjust the daily food of the patient so that there is sufficient nutrition to maintain bodily efficiency and prevent anemia. This may be carried out according to the principles already laid down. In addition, the intake of salt should be so regulated that the patient can eliminate it completely. This is a matter of individual adjustment either by observing the salt intake that causes a gain of weight, which is the most delicate index of incipient edema, or by determining the twenty-four-hour output of salt in the urine as the quantity in the diet is varied. It is remarkable how many individuals adapt themselves to an intake of 3 grams of salt a day and suffer no sense of privation after a very short time.

Uremia.—Broadly speaking, there are two types of uremia. The one is associated with marked retention of the substances that should be eliminated by the kidney, and is usually measured by the level of the urea or creatinin in the blood; the other occurs without any increase of urinary excretory products in the circulation, and while renal function is normal or nearly so. From the point of view of the physician the same treatment has been largely accorded both classes of uremia. It has been believed that in either case some toxic material was retained within the body, and that this must be eliminated. It is this side of the management that it is desired to take up here. Various symptoms, such as convulsions, restlessness, cardiac failure, acidosis, etc., must not be lost sight of, and treated symptomatically; however, the main point about which all ideas of therapy in uremia revolve is that of eliminative treatment.

What has been said of the diet and treatment of marked nitrogen retention under the heading of Urea and Creatinin of the Blood applies here as well, and need not be repeated. It is only necessary to accentuate the fact that a diet high in carbo-

hydrate and low in protein spares body protein and favors the complete elimination of nitrogen better than any other diet at our command. Furthermore, the starchy food serves to ameliorate some of the symptoms of acidosis, for this, because of retention, plays a rôle in most instances of uremia. In unconscious patients glucose solution in 10 per cent. concentration is borne well when given by stomach-tube.

It is always tempting to use diuretics and obtain the maximal kidney action. What has been said under Edema regarding these drugs applies in this condition. However, it is necessary to choose the most efficient renal stimulant if any attempt at all is to be made in saving life, since in very many uremics oliguria is the factor responsible for the course of events. Water furnishes the best means to bring this about. This may be given by mouth and forced to a certain extent (lemonade, orangeade, and water flavored with other fruits, milk in limited amounts, and almost any fluid desired may be used); if necessary the stomach-tube should be resorted to; fluid may be given by rectum either as 5 or 10 per cent. glucose, 5 per cent. soda bicarbonate, or normal saline solution; if it seems preferable, rectal irrigations of soda or normal saline may be employed; when enough fluid can be administered by mouth it seems superfluous to use infusions or hypodermoclyses.

The total amount of fluid administered in twenty-four hours should be at least 2500 to 3000 c.c. There are certain limits which the physical capacity of the body imposes. If there is a urinary flow, the intake can always be kept slightly in excess of the output; edema is no contraindication; in fact, these patients seem to do better when there is a subcutaneous accumulation of fluid; if hydrothorax does develop, it furnishes a very efficient means by which some of the toxic products may be removed. Although edema is no contraindication to forcing fluid, the cardiac embarrassment which may result therefrom must be closely looked out for and properly handled when it occurs. Infusions, especially glucose infusions, are the best emergency measures. Glucose in 10 to 20 per cent. solution and even higher is usually

borne very well.[1] Occasionally the amount of urine diminishes rather than increases when these procedures are instituted. There is no way to avoid this. It occurs in kidneys that are without any reserve force and fatigue easily. There is no other diuretic as bland and at the same time as efficacious as water; in cases in which this produces fatigue, the outlook is very poor. In the past too little fluid rather than too much has been used; some of the attempts that have been made to treat uremia have met with more or less success, not because of the drugs that were administered, but because of the large amount of fluid which acted as a vehicle.

In marked cases of uremia, bleeding is the measure which offers some hope of relief. Phlebotomy, however, should be employed with extreme reluctance and only after careful consideration of all the factors in the case. It usually furnishes the immediate solution of the problem in hand, but the after-effects, malnutrition and anemia, often spell ultimate disaster for the patient. The course of events reminds us of the common saying among the laity, that the operation was a success, but the patient died. Transfusion may possibly offset this drawback. I have tried it in desperate cases, and although no very great improvement occurred in them, yet there were no untoward symptoms entailed, and this measure may, if properly handled, offers some promise in the future. Plasmapheresis, the method of bleeding, centrifuging out and infusing the red blood-corpuscles, thus eliminating the plasma which is supposed to contain the toxic substances responsible for anemia, has up to the present not proved to be of value.[2] Bleeding followed by transfusion, easily as they are carried out today, would seem to embrace all the advantages of plasmapheresis and, in addition, do away with certain of the drawbacks of the latter procedure.

The time-honored methods of supplementing elimination by hot packs and other diaphoretic measures and by purging are

[1] Woodyatt, R. T., Sansum, W. D., and Wilder, R. M., Jour. Amer. Med. Assoc., 1915, lxv, 2067.

[2] O'Hare, J. P., Brittingham, A. B., and Drinker, C. K., Arch. Int. Med., 1919, xxiii, 304.

valuable adjuncts, and are as useful today as when they were first instituted.

Acidosis.—It is at present generally acknowledged that acidosis occurs in many cases of very severe nephritis as a result of insufficient kidney action.[1] This form of acidosis is radically different from some others, inasmuch as there is no overproduction of acid, but a deficient elimination, entailing an accumulation within the body. Marriott and Howland[2] have shown how an increase of phosphates within the body may be responsible for the condition, and how this is associated with marked renal insufficiency.

The treatment of acidosis in nephritis is in many respects like that of uremia, with which it is so often associated. The use of fluids in stimulating diuresis and starchy food to minimize protein metabolism is as strongly indicated here as there, and the details need not be repeated. Marriott and Howland have advocated the administration of calcium as an aid to the elimination of phosphates. This may be employed with impunity. Bicarbonate of soda as an alkali to relieve the situation should be used with caution. Since the kidney holds back the alkali, instead of an acidosis, an alkalosis, which is not in the least desirable, may follow. Either by noting the clinical symptoms, especially the depth of breathing, or what is much more preferable, judging by means of the CO_2 tension in the alveolar air or the quantity of carbonate in the blood, the amount of alkali administered is controlled. Unless the faulty eliminative power of the kidney is corrected there is usually very little hope, though an occasional marked case of nephritic acidosis can be saved even if only to live an invalid's life subsequently.

In the foregoing, one phase in the treatment of nephritis, that of retention, has been discussed. It is possibly this aspect of the disease that appeals to the clinician more than any other. However, there are other sides of this problem that are of equal if not greater importance. The finding of the cause and its eradication is beginning to receive the attention it deserves, and

[1] Palmer, W. W., Medical Clinics of North America, November, 1917, 659.
[2] Marriott, W. McK., and Howland, J., Arch. Int. Med., 1916, xvii, 708.

in a few instances has yielded brilliant success; the discovery of the nature of the toxic process that is responsible for many of the bodily changes, and possibly those in the kidney itself, still remains a matter of conjecture, and its control naturally cannot even be attempted. It is in work along these two lines that the greatest and real success in treating nephritis will come.

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RECURRING MENINGOCOCCIC MENINGITIS

Report of Seven Cases of Meningococcic Infection Recurring Within a Period of Four to Sixteen Weeks Following Recovery from the First Attack. Mode of Origin of the Second Attacks. Symptomatic Expression of the Pathology of These Second Attacks. Origins of Reinfection. Full Discussion of Treatment.

OF importance in connection with the general question of immunity to meningococcus infection is the study of recurrences, relapses, and reinfections. Two, three, and even more attacks of meningococcic meningitis in the same individual have been described. Usually these have occurred within a few weeks or months of the primary attack. Recurrences and recrudescences really form part of the irregular course of many prolonged cases and require no particular comment. Attacks occurring after longer intervals of time, intervals of several weeks or months, deserve special study because of their bearing on the question of immunity and upon the development of prophylactic measures. With this in view we report 7 cases of meningococcic infection recurring within a period of four to sixteen weeks following recovery from the first attack. Six of the 7 cases are 2.2 per cent. of an epidemic of 265 occurring at Camp Jackson, South Carolina. One is from the Base Hospital records of Camp Gordon, Ga., for which we are indebted to Dr. H. O. Mosenthal, formerly Captain, M. C., U. S. A.

CASE I.—The patient, W. A., No. 4773, was admitted to the Base Hospital January 12, 1918, with symptoms and physical signs of a severe cerebrospinal meningitis. Meningococci were found in the spinal fluid. Under active treatment, in which a total of 210 c.c. of antimeningococcic serum were given intraspinally and 45 c.c. intravenously, recovery ensued. During the course of the meningitis mumps developed from which the patient recovered without any complications. The patient became free from fever January 21st. He was discharged to duty on February 11, 1918, complaining only of stiffness in the right knee and showing exaggerated reflexes.

On February 25, 1918, the patient was re-admitted to the hospital with a history of sudden onset of severe headache, chill, and vomiting the day before. Examination determined the presence of a profuse petechial rash over the entire body. The skin was flushed and the ears cyanotic. Marked rigidity of the neck and positive Kernig's and Brudzinski's signs were present. All the deep reflexes were exaggerated. On lumbar puncture the cerebrospinal fluid was obtained under marked pressure and was reported to contain many pus-cells and many intracellular meningococci. Under active treatment, in which a total of 235 c.c. of antimeningococcic serum were given intravenously and 135 c.c. intraspinally, the symptoms and signs of meningitis gradually disappeared and the spinal fluid became normal. There remained, however, a persistent pain in the back over the site of the punctures, and limitation of motion of the lower extremities due to muscle spasm. After treatment for the latter condition in the orthopedic ward the patient was finally discharged to his command for duty.

CASE II.—This patient, C. H., No. 4993, was admitted to the hospital January 15, 1918, with a history of sudden onset of chilliness, slight headache, pain in the back, and fever. On the following day he showed a profuse hemorrhagic rash and the picture of a severe meningococcic infection; 45 c.c. of slightly cloudy spinal fluid were removed in which the meningococcus was found. The blood-culture was negative. Under treatment,

in which a total of 180 c.c. of antimeningococcus serum were given intraspinally and 60 c.c. intravenously, complete recovery occurred. The only complication was arthritis of the right knee. On March 12, 1918, after having had a normal temperature from January 26, 1918, he was discharged to duty apparently in complete health.

On March 16, 1918, four days after discharge from the hospital, the patient was re-admitted complaining of occipital headache and weakness. The temperature was 99.4° F. and the neck slightly rigid. No other signs or symptoms were noted. The general condition remained the same until March 18th, when increased rigidity of the neck, slightly positive Kernig's and Brudzinski's signs were found. On lumbar puncture 10 c.c. of clear fluid were removed, which was reported to contain 400 cells per c.c., increased globulin, and a few Gram-negative intracellular diplococci. After the patient was desensitized 135 c.c. of antimeningococcic serum were given intravenously and 30 c.c. intraspinally. The next day a right facial paralysis developed. Active treatment by intravenous and intraspinal injection of antimeningococcic serum was continued. The patient did not respond to treatment, became progressively worse, and died March 29th, thirteen days after the recurrence of symptoms.

At necropsy, March 29, 1918, the central nervous system alone was examined. Brain: On opening the dura there was escape of a large amount of cerebrospinal fluid. The brain was dark in color from congestion of the superficial blood-vessels. There was slight flattening of the convolutions and a small amount of pus over the upper part of the brain. Thick, purulent exudate covered the under surface of the brain. There was a large amount of fluid in the lateral ventricles and in the fourth ventricle.

CASE III.—The patient, G. C., No. 3843, was admitted to the hospital December 25, 1917, with history of a sudden onset of severe frontal headache, chill, and vomiting a few hours before admission. Examination determined the presence of symptoms and signs of a moderately severe meningitis. On lumbar puncture cloudy cerebrospinal fluid under marked pressure was re-

moved. It contained many pus-cells, but no micro-organisms. The patient was treated with intraspinal injections of anti-meningococcus serum only, and the symptoms and signs of the meningitis gradually disappeared. There was acute cellulitis of the palmar surface of the left hand with abscess. A marked and persistent weakness of the right forearm and a slight bilateral deafness resulted from the attack. During this primary attack the fever lasted but four days. Convalescence, however, was prolonged and marked by vertigo, weakness, deafness, and exaggerated reflexes. On February 13, 1918, the patient was transferred to the orthopedic ward.

On February 17, 1918, the patient suddenly developed again the clinical picture of meningitis. Marked rigidity of the neck, Kernig's and Brudzinski's signs were present. On lumbar puncture 60 c.c. of cloudy fluid were removed, which contained numerous pus-cells but no micro-organisms. A very stormy period ensued in which the patient had maniacal attacks, extreme opisthotonus, and a temporary paralysis of the bladder. There was delirium and a psychosis with hallucinations and delusions, great loss of weight, and development of an acute hydrocephalus. At one time the patient ceased breathing. First Lieut. S. A. Cobb, M. R. C., performed immediate spinal puncture and manipulated the head vigorously upon the neck. After a few moments there was a sudden spurt of spinal fluid through the needle under great pressure, and at once breathing was renewed. Spinal punctures were repeatedly made and active treatment with intravenous and intraspinous injections of anti-meningococcic serum was given. The meningococcus was demonstrated in the cerebrospinal fluid for the first time on February 26, 1918. The cerebrospinal fluid changes as well as the clinical picture of meningitis persisted until March 12th, when improvement began and continued until entire convalescence.

CASE IV.—The patient, T. W., No. 7918, was admitted to the hospital March 18, 1918, with a history of sudden onset, on March 12th, of frontal headache, chill, vomiting, and pains in the head and neck. On admission the temperature was

103° F., the pulse 100. The patient was unconscious, unable to answer questions, slightly delirious, and vomiting. He was weak and pale and in poor general condition. There was stiffness of the neck, positive Kernig's and Brudzinski's signs, and an extensive petechial rash. On lumbar puncture 30 c.c. of cloudy fluid were removed under marked pressure. It contained many pus-cells and a few Gram-negative diplococci; 20 c.c. of antiserum were injected intraspinally and 120 c.c. intravenously. In thirty minutes a marked urticarial rash appeared over the whole body. The patient was in very poor condition.

On March 14th the patient was conscious, rational, and drowsy. The general condition was very much improved.

Under further active treatment, in which a total of 385 c.c. of antimeningococcus serum were given intravenously and 75 c.c. intraspinally in a period of three days, the spinal fluid became clear and the symptoms subsided.

On March 22d the patient was up and about without complaint, excepting weakness.

On March 26th the patient vomited during the night, had a chill and very severe headache, with a temperature of 99⅘° F., and a pulse of 104. There was rigidity of the neck and exaggerated reflexes, but no rash. By lumbar puncture 55 c.c. of very cloudy fluid under marked pressure were removed. Active treatment was again started, and in two days, during which 120 c.c. of serum were given intravenously and 50 c.c. intraspinally, convalescence was again established and the patient was later transferred to the Convalescent Division.

He was entirely free from fever March 26th to May 23d. On April 13th a note stated that all the deep reflexes were exaggerated and equal except that the right abdominal was more active than the left. The patient complained of slight pain in the right hip. He was unable to bend forward because of stiffness of the lumbar spine.

On May 23d there was recurrence of fever to 101.2° F., with headache, rigidity of the neck, and vomiting. On lumbar puncture cloudy cerebrospinal fluid under pressure was removed. It was reported to contain many pus-cells and no organisms.

A blood-culture taken at this time was negative. Treatment with antimeningococcus serum, of which a total of 490 c.c. were given intravenously and 155 c.c. intraspinally, resulted in a return of the cerebrospinal fluid to normal and a subsidence of the symptoms within six days, except a residual weakness and slight atrophy of the lower extremities, with vasomotor disturbances and painful cramps—the undoubted result of local meningitis, local irritation from serum, and repeated lumbar puncture.

CASE V.—The patient, C. R., No. 6230, was admitted to the Base Hospital February 5, 1918, with a history of having had on the previous evening a chill followed by headache and later vomiting. On admission he was acutely ill, with dyspnea and cyanosis present. The skin showed numerous petechial spots. He had rigid neck, a positive Kernig's and Brudzinski's sign, and absent patellar and Achilles' reflexes. The temperature was 103° F. and the pulse 84. On lumbar puncture 60 c.c. of milky fluid were withdrawn, which was reported to contain many pus-cells, but no organisms. Under active treatment with antimeningococcus serum, of which a total of 180 c.c. were given intravenously and 85 c.c. intraspinally, a prompt subsidence of the clinical symptoms of meningitis and return of the fluid to normal occurred. At no time were meningococci found in the cerebrospinal fluid. The blood-culture was negative. One week after the initial symptoms of meningitis the patient was convalescent. He was discharged to duty March 2, 1918.

On June 28, 1918, the patient was re-admitted to the Base Hospital with a history of having been seized the day before with frontal headache, nausea, and vomiting. On admission he was acutely ill and complained of severe frontal headache. The mentality was not impaired. A roseolar, macular rash was present on the upper chest and a few scattered petechiæ were present on the shoulder and the pelvic girdle and on the abdomen and lower extremities. The neck was rigid and the tendon reflexes were exaggerated and ill-balanced. Kernig's and Brudzinski's signs were positive. On lumbar puncture 70 c.c. of cloudy fluid were withdrawn under marked pressure. It was

reported to contain a few Gram-negative diplococci and many pus-cells. The blood-culture was positive for meningococci. Under active treatment, in which a total of 580 c.c. of antimeningococcic serum were given intravenously and 180 c.c. intraspinally, a prompt subsidence of the symptoms of meningitis followed, with a return of the spinal fluid to normal. The patient made an ordinary convalescence.

CASE VI.—J. H. W. This soldier was admitted to the Base Hospital March 23, 1918, with a history of severe headache, nausea, and vomiting. There was rigidity of the neck and the reflexes were hyperactive. He had a general macular eruption and numerous definite petechial hemorrhages over the body. The spinal fluid on admission was in amount 40 c.c., clear, and under increased pressure contained a large number of pus-cells, but no organisms. On March 25th 40 c.c. of similar fluid were withdrawn. Two intravenous injections of antimeningococcic serum of 90 c.c. each were given. He had a temperature for four days and made an uneventful recovery. Organisms were never demonstrated in the spinal fluid or blood, but the case was clinically positive for meningococcic meningitis.

Upon convalescence this soldier was transferred to Camp Greenleaf, Ga., where on April 26th he was taken with a chill, a severe headache, nausea, and vomiting. He was admitted to the General Hospital No. 14, Fort Oglethorpe, Ga., April 27, 1918, with severe headache, nausea, vomiting, marked rigidity of the neck, hyperactive reflexes, a macular eruption, and many petechial hemorrhages over the body. Kernig's sign was positive. In addition, cloudy spinal fluid was removed under pressure, the cell count being 4500. Microscopic examination revealed Gram-negative intracellular diplococci, which were also recovered on culture. The cerebrospinal fluid of April 28th showed similar findings. By May 4th the meningococci had disappeared from the cerebrospinal fluid. On June 28, 1918, soldier was returned to duty, and on July 13, 1918, he was in good physical and mental condition. No note of temperature in the two attacks is available.

CASE VII.—B. F., No. 34,479, Base Hospital, Camp Gordon, Ga. Patient states that he had spinal meningitis while in France; that he was unconscious for six weeks; that his spine was tapped twenty-six times; that he was given serum about thirty-three times, and was not out of bed until December 18, 1918, and that he had a left squint at convalescence. On March 2, 1919, after being returned to Camp Gordon, the patient had chills, fever, headache, and general malaise, and on March 4, 1919, he was admitted to the hospital in a hysteric condition, throwing himself about and moaning; his neck was rigid, the knee-jerks were absent, and there was no Kernig's sign. There was a left external strabismus, pupils equal, and reacted to light. Lumbar puncture revealed a turbid fluid with a pure culture of Gram-negative diplococci. Organisms were also found on smear; globulin three plus, cell count 720. Recovery was prompt with intraspinal and intravenous serum treatment.

Discussion.—The mode of origin of these second attacks is important. They may be considered reinfections from without or from within. While the former is possible as a result of infection with a different type of meningococcus, as suggested by Professor Zinsser, the latter seems more probable. In his discussion of reinfection of the meninges Dr. Flexner remarks that this arises doubtless "from some protected, because little accessible, active focus in the meninges or ventricles." Necropsies of prolonged cases or of convalescents from meningitis dying from other diseases throw light on the source of these reinfections. The meningococcic exudate in the subarachnoid spaces is absorbed slowly. It undergoes a mucoid or gelatinous transformation and for several weeks after active symptoms masses of rather clear, jelly-like substance mixed with more or less organized fibrinopurulent exudate may be found over the base of the brain, about the lumbar part of the spinal cord and cauda equina, less frequently on the choroid plexus and in other parts of the ventricles. Such slowly absorbing exudate is probably the cause of the persistent symptoms following ordinary cerebrospinal meningitis. Vasomotor disturbances, headache, emotional instability, muscular weakness, poor nutrition, altered reflex activity may all be symptomatic expressions of this pathology.

In addition to this more or less expected meningeal condition, foci in which meningococci may be walled off and from which reinfection may arise are the accessory sinuses of the nose which at necropsy frequently contain pus with meningococci. The joints, the pericardium, the eye, the middle ear may act in a similar way as origins of reinfection. A certain amount of general systemic disturbance may result from a persistent focus of infection in any of the regions named. With local treatment of these lesions by serum or by surgical measures these symptoms promptly disappear. One of the important duties of the medical attendant is the search for and the appropriate dealing with such local residuals.

It is of further interest to note that with the possible exception of Case VI these 7 cases with recurrent attacks were very ill with the primary attack, and had abundant serum treatment, to which they responded satisfactorily. No second attack occurred in an abortive case or in one which did not receive what is now considered by us an adequate amount of specific antiserum. An explanation of the lack of lasting immunity in these cases suggests itself. Immunity in individuals treated with large amounts of antiserum is largely if not entirely passive. In the presence of a readily available antibody the specific antibody-producing mechanism of the patient's own tissues may not be called into play, but may remain idle. With the excretion or destruction of the borrowed antibody numbers of less accessible or more resistant meningococci which have been restrained from activity by the presence of the hostile substances may again invade the tissues, which, because they have not been called upon actively to repel the invader, are not well prepared to deal with it. In brief, passive immunization carries with it the menace, however remote, of recurrent attacks.

A logical basis for the use of vaccines during convalescence is thus established. The active immunity, doubtless gained by their use, would seem to reduce the liability to recurrences. Three to five injections at five-day intervals of 50,000,000 to 200,000,000 killed meningococci, preferably "autogenous" or at least of the same type as that harbored by the patient, are to be advised.

CLINIC OF DR. ARTHUR F. CHACE

POST-GRADUATE HOSPITAL AND MEDICAL SCHOOL

THE VALUE OF CHEMICAL BLOOD EXAMINATIONS IN DIAGNOSIS, PROGNOSIS, AND TREATMENT OF SOME CONSTITUTIONAL CONDITIONS

With Presentation of Illustrative Cases of Acidosis, Uremia, Interstitial Nephritis, Essential Hypertonia, and Parenchymatous Nephritis.

October, 1919.

IN order to emphasize the importance of chemical blood examinations to the general practitioner 5 illustrative cases will be presented. The first case is one of *acute acidosis in nephritis*, showing the importance of testing the carbon dioxid content of the blood; the second, one of *uremia*, demonstrating the value of creatinin determination in the blood as a prognostic sign; the third, a case of *essential hypertonia*, demonstrating the importance of estimating the amount of nitrogenous retention in the blood in order to establish the diagnosis as distinguished from that of interstitial nephritis; the fourth, a case in which a diagnosis of essential hypertonia had been made clinically, but which, from the laboratory reports of the blood, proved to be a critical case of *interstitial nephritis;* and the fifth, a case of pure *parenchymatous nephritis*, in which the diagnosis was established and made favorable by the demonstration of a lack of retention of nitrogenous waste products in the blood.

You will recall that the normal findings in the blood are as follows:

Urea.	Uric acid.	Creatinin.	Sugar.	CO_2 (Van Slyke method).
15	2	2	0.1	50

The blood findings in each case presented will be copied on the blackboard underneath these figures, for purposes of ready comparison.

The first patient, who has kindly consented to come here, does not look as he did upward of three years ago, when he was brought to the hospital, unconscious, with a history of having had convulsions. At that time he presented the clinical appearance of a patient in coma, with a rapidly fatal prognosis.

CASE I.—W. A. C., aged forty-nine, Irish, an agent by occupation, admitted to the hospital January 15, 1916, with a history that he had been treated for influenza for five days before admission to the hospital; that he had been confined to bed with headache, drowsiness, and some impairment of vision; that two days before admission dyspnea developed, the urine was examined, and the patient told that he had kidney trouble; that he completely lost his sight the day before coming to the hospital, and on that afternoon was found in convulsions biting his tongue.

Previous History.—His friends stated that for the past six months he had suffered from nocturia and insomnia, that for three weeks he had complained of palpitation, headache, and a slight cough, and that for two weeks his vision had been impaired and be had suffered from dyspnea and vertigo. His friends said that he had been drinking heavily and had complained of loss of appetite and vomiting after taking food.

Physical Examination.—Revealed cyanosis, dyspnea, twitching of muscles, edema of eyelids and scleræ, lips blue, tongue swollen, orthopnea, pulmonary congestion posteriorly, myocarditis, and edema over the sacrum. There was no edema of the extremities and no rigidity of the neck. His blood-pressure was 210.

Laboratory Findings.—Upon admission the urine was greatly decreased in amount, contained a trace of albumin and numerous hyaline, granular, and waxy casts. On successive urinary examinations a moderate amount of albumin was found, as well as a few casts. The blood showed secondary anemia with a slight leukocytosis. The phenolsulphonepthalein test was 38

and 55 on two examinations. The Wassermann reaction was negative.

Blood Chemistry:

	Date.	Urea N.	Uric acid.	Creatinin.	Sugar.	CO_2 (Van Slyke method).
	1/15/1916	44	9.5	3.5	.....	22
	1/17/1916	62	...	4.1	.....	58
	1/18/1916	42	5.6	2.0	0.152	56
	1/19/1916	53	4.3	3.2	0.120	54
	1/28/1916	19	2.5	1.9	0.140	
	2/1/1916	19	2.8	2.0	0.150	
(After dis.)	5/26/1916	12	4.5	1.8	0.135	
(After dis.)	6/11/1918	16	4.4	1.8	0.150	

The CO_2 content of 22 in the blood established the diagnosis of acidosis and indicated the form of treatment.

Diagnosis.—Acute acidosis occurring in an acute exacerbation of chronic interstitial nephritis.

Course and Treatment.—A phlebotomy was performed, 100 c.c. of blood being withdrawn, and 400 c.c. of a 2 per cent. solution of sodium bicarbonate administered intravenously as an infusion. This treatment was repeated the following day. A lumbar puncture was done the second and third days; the fluid was under increased pressure. The patient resumed consciousness after the first infusion. He was given 1 dram of sodium bicarbonate by mouth four times a day, and also daily colonic irrigations of a 3 per cent. bicarbonate of soda solution, allowing 1 pint of this solution to be retained. Not only did the patient resume consciousness, but the CO_2 content of his blood returned to normal, as shown in the above table.

For the first three days after becoming conscious he received the following diet: Juice from 1 lemon, ⅔ cup of water, 6 tablespoons of lactose (1 tablespoon of cane-sugar), served four times a day. This diet provides 1424 calories, contains 0.8 mg. of iron, and furnishes the requisite amount of alkaline ash. Subsequently, it was somewhat enlarged, and he was permitted cocoa, bread and butter, cereals, vegetable soup, baked potato, and rice—the usual low protein diet given to avoid albuminuria.

The patient showed a gradual and steady improvement, and was discharged on the twenty-ninth day.

Remarks.—Here is a patient who was brought to the hospital in coma following a convulsion, clinically uremic, but from the blood examination shown to be complicated by a severe acidosis. From the clinical findings and typical history the prognosis certainly looked bad, and had it not been for the results obtained in the chemical blood examination, an unqualifiedly bad prognosis would have been given.

The significant point of his blood chemistry was that although he was retaining a quantity of nitrogenous waste products, it was not a fatal amount. Our experience has shown that patients with less than 5 mg. of creatinin in the blood recover, and that those having more than 5 mg. generally end fatally. A clue to the treatment was obtained by finding only 22 CO_2 content in the blood, which showed the case to be one of extreme acidosis. Patients with less than this amount usually die. In other words, the finding of a moderate amount of nitrogen retention with a very marked acidosis indicated a relatively favorable prognosis, and also showed the immediate necessity of administering large quantities of alkalies.

Before his discharge the patient had a normal blood chemistry, the acidosis having been neutralized. For about six weeks after discharge the low protein diet was continued, and since that time (about three years and nine months) the patient has been doing very much as he pleases, even smoking and drinking. He has been perfectly well during all this period, and has not had an attack.

In passing, it may be said that dyspnea is a cardinal symptom of acute acidosis; the digestive upsets are not diagnostic, as they are met with in other conditions. In fact, it is safe to say that unless attributable to heart decompensation, the dyspnea in advanced nephritis is practically always indicative of acidosis. This point has an important bearing on the treatment. The dyspnea of nephritis may be relieved by giving alkalies until the acidosis is overcome.

CASE II.—The second case is one of *chronic uremia*, which proved fatal. The history is as follows: J. W., aged thirty-four,

Irish, a clerical worker by occupation, admitted to the hospital February 22, 1915, complaining of dyspnea, headaches, insomnia and blurring of vision, constipation, occasional nausea and vomiting, all of about fifteen months' duration, during which time he was unable to work. For three weeks before admission the headaches were almost unbearable, worse at night, and the dyspnea gradually became exaggerated. He also complained of nocturia and marked polyuria.

Previous History.—The patient gave a history of having contracted syphilis sixteen years previously, which had been treated effectively; his Wassermann reaction was now negative.

Family History.—Negative.

Physical Examination.—Revealed a man of anemic, waxy appearance, with mucous membranes pale, conjunctivæ pale, albuminuric retinitis, and coated tongue. The second aortic sound was accentuated, the radicals were thickened, and there was a slight systolic murmur with maximum intensity over the second aortic area.

Laboratory Findings.—The urine was of low specific gravity, pale, with a moderate amount of albumin and granular casts, as well as an occasional hyaline cast. There was a constant polyuria of between 3000 and 4000 c.c. in twenty-four hours. The blood was normal except for a slight leukocytosis. The sputum and Wassermann were negative. Phenolsulphonephthalein test showed 3.6 per cent. at first and later only a trace.

Blood Chemistry:

Date.	Urea N.	Uric acid.	Creatinin.
2/24/1915	55	8.1	8.3
3/1/1915	63	5.6	6.5
3/6/1915	89	6.0	5.3
3/19/1915	51	4.2	6.5
3/25/1915	51	7.0	6.1
4.8/1915	61	7.2	8.0
4/14/1915	Uremic coma		
4/15/1915	144	8.7	11.0
4/16/1915	Death		

Diagnosis.—Chronic interstitial nephritis terminating in uremic coma. During his stay in the hospital the pulse was regular.

The blood-pressure varied between 225 systolic and 100 diastolic as extremes.

Course and Treatment.—Upon admission the patient was placed upon a diet rich in milk, cereals, vegetables, and cooked fruits, containing 40 grams of protein, alkaline ash 59 n., and 15 mg. of iron, furnishing 2278 calories. When the nitrogen in his blood increased, the protein content in the diet was further reduced, giving him at times a cornstarch blanc-mange diet, consisting exclusively of carbohydrates.

It was interesting to note that the creatinin and urea in his blood would drop when upon this very restricted diet; however, it was always impossible to reduce the creatinin below 5.3.

In addition to the dietary régime he received the standard symptomatic treatment for uremia, including colonic irrigations and general hygienic measures.

Remarks.—Mr. W. attracted particular interest inasmuch as he was referred to the hospital as a case of gastro-enteric disorder. He had been treated symptomatically for nausea, vomiting, constipation, and bilious headaches. He considered himself primarily a stomach case. The fact that Mr. W. was suffering from chronic uremia was first noted by the laboratory in their routine chemical blood examinations. They made a fatal prognisis after their first examination which showed a creatinin content in the blood of 8.3 mg. The patient so greatly improved under treatment that he wished to leave the hospital and resume his former occupation, and in order to keep him in the hospital under observation he was given the work of an orderly. He constantly protested that he was perfectly well and should get to work. After being in the hospital about two months, without any apparent cause he suddenly developed uremia, and died in uremic convulsions within forty-eight hours.

The gravity of this case would not have been appreciated had it not been for modern laboratory methods. Before the era of blood chemistry many cases of this character were discharged from the hospitals markedly improved, and then suddenly develop a fatal uremic convulsion a few days after going home. Some

of the cases with "death undetermined" undoubtedly belong in the category of unrecognized cases of uremia.

CASE III.—The third case is presented to demonstrate the importance of chemical blood examinations in making an accurate prognosis in cases of high blood-pressure.

H. B., aged thirty-eight, married, Irish, housewife, admitted to the hospital October 1, 1917, complaining of hot flashes, vertigo, headaches of increasing severity, particularly in the occipital region. The patient also suffered from obstinate constipation and general abdominal distress. She was neurotic, excitable, and given to worrying. All of her symptoms were intermittently progressive over a period of three years.

Previous History.—For seventeen years previously the patient had suffered from nervousness, and had had frequent nervous headaches with considerable gastro-intestinal disturbances, consisting of hyperacidity and constipation.

Family History.—Negative.

Physical Examination.—Revealed teeth poor, with several missing, tongue clean. The heart was enlarged to the left 3 cm.; sounds at the apex accentuated, P_2 accentuated and greater than A_2. Lungs and abdomen were negative. Varicose veins of the legs, particularly on the left. The eyes showed temporal pallor and congestion of nasal side; the retinal vessels were of normal caliber, tortuous, deep carmin in color; the choroidal vessels were moderately congested. An ocular diagnosis of bilateral retinal venous hyperemia with no evidence of arteriosclerosis was made.

Laboratory Findings.—Aside from an occasional faint trace of albumin, the urine was normal throughout her stay in the hospital. The phenolsulphonephthalein output was practically normal. The blood was normal. Examination of the stools and Wassermann reaction were both negative.

Blood Chemistry:

Date.	Urea N.	Uric acid.	Creatinin.	Sugar.
10/5/1917	14.1	5.5	3.1	0.126

Diagnosis.—Essential hypertonia without evidence of interstitial nephritis. (The excess of uric acid in the blood might indicate an incipient nephritis.)

	Date.	Systolic.	Diastolic.
Blood Pressure:	10/1/1917	258	514
	10/4/1917	245	150
	10/5/1917	250	140
	10/7/1917	240	120
	10/9/1917	170	100
	10/12/1917	175	110

Course and Treatment.—The patient received the regular hospital diet, saline catharsis, warm baths, rest, and nerve sedatives. On this régime her symptoms improved, and she was discharged from the hospital after a two weeks' stay, feeling well, with a systolic blood-pressure of 175, and a diastolic of 110.

Remarks.—The prognosis and treatment in this case depended upon the phthalein test and the blood findings. It would have been impossible to have promised this patient a favorable prognosis without the evidence of no retention of nitrogenous waste products in the blood, and particularly a normal phthalein output. The severity of the symptoms would have been the same in chronic interstitial nephritis as in essential hypertonia, and a differential diagnosis would not have been possible. Without a positive assurance of no kidney involvement the patient would have been placed upon an unnecessarily restricted diet.

In this connection an incident which occurred some years ago in the practice of a prominent physician here in the city may be of interest. He was consulted by a man about sixty for essentially the same symptoms as this case presents, who was accustomed to going off on his yacht for weeks at a time, drinking and smoking heavily. The physician gave him the customary advice, adding that unless he reformed his ways, gave up alcohol, got plenty of sleep and lived a moderate sane life, he would die within a year. Some four years later the physician met the man and inquired concerning his health. The patient told him that the advice had not been followed, remarking that he was "still here." Such an error in prognosis could not have occurred

had nephritis been eliminated from the diagnosis, and its non-existence could have been ascertained by obtaining the blood chemistry. That patient certainly would have died within the year had he been retaining nitrogenous material in his blood, as seemed to be indicated by the symptomatology and blood-pressure.

In instances such as these guidance is absolutely essential not only in order to determine the significance of a high blood-pressure and its accompanying symptoms, but to outline the necessary treatment, and the blood chemistry is the only method of diagnosis that furnishes a proper guide.

CASE IV.—The following case illustrates the difficulty in differential diagnosis between essential hypertonia and chronic interstitial nephritis.

C. H., aged fifty-two, married, German, salesman by occupation, admitted to the hospital September 25, 1919, complaining of distress in the stomach, consisting chiefly of pyrosis, regurgitation and discomfort after eating; dyspnea on exertion, palpitation; occasional slight edema of ankles; loss of weight, nocturia; all symptoms intensified during past five months.

Previous History.—Diphtheria, mumps, and tonsillitis in childhood. For twenty years patient had been having attacks of weakness, vertigo, headache, and nausea, usually lasting four to five hours, and terminating in severe vomiting. About five years ago these attacks ceased, and the stomach disturbances noted above commenced; during these five years he had been treated for duodenal ulcer.

Family History.—Father died at seventy-one of dropsy, and one brother died at thirty-five of acute nephritis.

Physical Examination.—Showed the heart slightly enlarged to the left and heart sounds faint; high tension pulse compressed with difficulty; the blood-pressure on two succeeding examinations was systolic 230, diastolic 138, and systolic 222, diastolic 120. The eye-grounds showed hemorrhagic retinitis.

Laboratory Findings.—The urine was negative except for a large amount of albumin. *x*-Ray of the gastro-intestinal tract failed to reveal anything save hyperperistalsis, and delayed in-

testinal hypomotility. Analysis of the gastric contents showed retention (none expressed), total acidity of 60 (Ewald), free HCl of 11, with a combined acidity of 28, and no blood or lactic acid.

Blood Chemistry:

Date.	Urea N.	Uric acid.	Creatinin.	CO_2 (Van Slyke method).
10/7/1919	44	5.1	6	55

Diagnosis.—Interstitial nephritis (determined 10/7/1919—today).

Treatment.—The patient will now be advised to take a low protein diet consisting of about 40 grams of vegetable and milk proteins, and made up largely of vegetables, cereals, cooked fruits, and milk. Elimination through the intestinal tract will be encouraged and his kidneys protected in every way.

Remarks.—This patient has been selected to be presented to the class as a case of essential hypertonia. The gastro-intestinal tract had been completely eliminated as the seat of the trouble by the *x*-ray and laboratory findings. In order to make the case complete a chemical blood examination was made this morning, and, much to our surprise, a retention of 6 mg. of creatinin was found, together with an increased amount of urea. This fact alters the diagnosis, prognosis, and treatment. He must be treated as a case of pure nephritis and given an unfavorable prognosis.

CASE V.—The fifth case is one of *parenchymatous nephritis*, in which the diagnosis was confirmed by means of the chemical blood examination.

N. M., aged twenty-nine, Italian, junkman by occupation, admitted to the hospital June 3, 1919, complaining of gradually increasing weakness for the past six months, loss of weight, loss of appetite, occasional pyrosis, dyspnea on exertion, pain in the back, nocturia, and swelling of feet, legs, arms, hands, and face increasing on overeating or using salt in the food. He also suffered from frontal headaches. These symptoms were of six months' duration and progressive.

Previous History.—This was negative save for the fact that two years ago patient had suffered from edema, dyspnea, cyanosis, and coldness of extremities, which had responded well to treatment.

Physical Examination.—Showed the tongue to be heavily coated and the breath fetid. The heart was slightly enlarged downward and to the left, P_2 accentuated, and roughening of the first sound at the apex. Slight edema of the ankles.

Laboratory Findings.—The urine was slightly low in specific gravity of normal, with a variable amount of albumin, granular and hyaline casts, and white blood-cells. The blood showed a moderately severe secondary anemia. The Wassermann reaction was negative. The phenolsulphonephthalein output was as follows:

	Per cent.		Per cent.
6/6/19	23	7/5/19	51
6/31/19	41	9/2/19	52
7/1/19	61		

Blood Chemistry:

Date.	Urea N.	Uric acid.	Creatinin.	Sugar.
6/5/19	22.9	.....	1.9	0.102
6/17/19	22.2	.....	1.7	0.103

Day and Night Excretion of Nitrogen and Chlorids—9/13/19.

	Vol.	Sp. gr.	Nitrogen.			Chlorids.		
			Gm.	Per cent.	Concent.	Gm.	Per cent.	Concent
Day	280 c.c.	1028	2.93	27.5	1.04	0.56	27.7	0.20
Night	565 c.c.	1020	7.68	72.5	1.35	1.46	72.3	0.26
Total	845 c.c.		10.61			2.02		

The blood chlorid on 10/7/19 was 0.630 per cent.

Diagnosis.—Chronic parenchymatous nephritis.

Course and Treatment.—The patient was placed upon the standard parenchymatous diet, with all food salt free, consisting of cocoa, milk, matzoths, butter, cereals, such as cream of wheat or rice, baked potato, sugar, cream, and stewed prunes or apricots. This diet contains protein, 49.52; fat, 103.91; carbohydrates, 352.56, and furnishes a total of 2414 calories, with a nutritive ratio of 1 : 9.3. Fluids were restricted. The pa-

tient is still in the hospital and has shown a gradual but steady improvement.

The important point in the dietetic treatment is the limitation of the intake of salt and water. It is not only unnecessary to restrict the intake of protein, but an increase in the amount of protein is actually indicated in certain instances, more particularly in those cases in which the blood becomes so impoverished in its content of serum albumin and serum globulin that edema results. In cases of severe anemia a rapid administration of protein by means of a blood transfusion is advisable.

Remarks.—In a case like N. M. it is important to know whether the patient is having primarily a parenchymatous nephritis, or complicated with it an interstitial nephritis. Are the kidneys unable simply to eliminate salt and water, or are they impermeable also to nitrogenous waste products? With salt and water retention only the prognosis is good and no restriction of ingested protein is necessary, but with the retention of nitrogen the prognosis is less favorable and a diet restricted in protein is important. The phthalein output, as noted in the table, varied from 23 to 61 per cent.

SUMMARY

In concluding, the following points should be emphasized: (1) The estimate of the carbon dioxid content of the blood in all suspected cases of acidosis, particularly where dyspnea is a prominent symptom. (2) The testing of the blood for the amount of creatinin as a prognostic sign in cases of uremia. (3) The diagnostic determination between essential hypertonia and chronic interstitial nephritis by examining the blood for the amount of nitrogenous waste products. (4) The analysis of the blood for its salt content in establishing the diagnosis of uncomplicated parenchymatous nephritis.

CLINIC OF DR. GEORGE STUART WILLIS

POST-GRADUATE HOSPITAL AND MEDICAL SCHOOL

RADIUM THERAPY

The Physiologic Action of Radium. Cases Illustrating the Value of Radium Treatment

October, 1919.

GENTLEMEN:

As a preliminary to our clinic today I will give a brief history of radium and its relation to medicine. The discovery of radium was not a mere accident or a chance chemical discovery; its evolution was dependent upon much scientific effort, beginning many years ago. To Lenard the credit must be given for the opening of this new chemical progress, and his work on the cathode rays was undoubtedly productive of enough interest to have stimulated the discovery of the *x*-ray by Roentgen in 1895.

The rays given out from a vacuum tube through which a charge of electricity is being passed brought to the minds of a number of chemists the fact that similar rays were spontaneously given off from certain known minerals. The initial work on this subject of radio-activity was done on the uranium group, and it will be remembered that about the year 1898 the world was much interested in the announcement of the discovery of a new element which Madame Curie and her husband had isolated and named radium.

History teaches us that every new discovery has always met with adverse criticism. The isolation of radium from uranium was no exception to this rule, and since its use in medicine has been possible a great deal of our knowledge has been shrouded in fakism and mystery.

From the medical standpoint our knowledge is still very limited. This is not to be wondered at, because of the marvels of this element which have completely revolutionized physics and chemistry. It is too vast a subject to have been perfected in so short a time. Radium was first commercially isolated from pitchblend obtained from the Austrian mines. It is said that this source of supply was rapidly exhausted and after ineffectual efforts to obtain pitchblend from the Cornwall tin mines notice was taken of an ore named after Carnot, a former President of the French Republic. This ore, carnotite, is found in the Paradox Valley, Colorado, and contains a combination of uranium, radium, and vanadium.

Until 1910 the mining of this ore was of particular interest for its vanadium content, the vanadium being extracted and used as a ferro-vanadium alloy in the manufacture of vanadium steel. Until 1910 carnotite had been shipped from our Colorado mines to France, England, and Germany, where the radium was also extracted and sent back to this country and sold at tremendous profits. Later, companies were formed in this country, and at the present most of the radium for the world market is extracted here.

For a time after its isolation radium was of interest merely from a physical and chemical standpoint, and it has been stated that the reaction caused by carrying a tube of radium in his pocket was what first attracted Becquerel's attention to its possible use as a destructive agent in the treatment of cancer. Rutherford says: "The term 'radio-active' is applied to a class of substances such as uranium, thorium, radium and its compounds, and these possess the property of spontaneously emitting radiations capable of passing through plates of metal and other substances opaque to light." They also have the secondary action of affecting a photographic plate and the power of discharging electrified bodies.

The alchemists of the Middle Ages believed in the transmutation of the elements; in other words, they believed it possible to transform elements from one chemical class into another. In those days lead, silver, and copper were all spoken of as "impure

gold." Their theories of transmutation have aroused wide interest in future possibilities, and the powers of radium through atomic transformation into different substances have led many chemists to believe that these old writings may sometimes be recognized as prophecies.

Uranium, the mother of radium, has an atomic weight of $238\frac{15}{100}$, and the period of its average life is estimated at eight billion years. Pure uranium freshly prepared emits a feeble alpha radiation and disintegrates into Uranium II. This has an atomic weight of 234. This element is supposed to have a life period of two million years. Uranium II disintegrates into uranium X. The life of uranium X is 35.5 days. Uranium X is supposed to disintegrate into ionium; the life of this element is supposed to be about one million years. At present we know very little about it, but its disintegration product is radium. The atomic weight of radium is 226, and its life period is about twenty-five hundred years. We may add that if radium had no powers of disintegration it would be of very little value to us from a medical standpoint, as radium itself is practically rayless. From the first disintegration product of radium—the emanation—we attain all its therapeutic values. Radium is constantly disintegrating this gas, known as "Emanation," the life of which is about five and fifty-five-hundredth days, and from this we obtain alpha rays.

The emanation disintegrates into what is known as the "active deposit of rapid change," and from radium A, B, and C we obtain our Alpha, Beta, and Gamma rays, the activity of which gives our entire therapeutic action in disease. Further disintegration products are known as radium D, E, and F, and are spoken of as "the active deposit of slow change." To illustrate: I am holding on this platter a tube of radium containing 100 milligrams of radium bromid. The salts used in the treatment of disease in combination with barium are bromid, chlorid, carbonate, and sulphate. With proper protection we may use radium in two ways: first, by applying the radium tube directly to the surface to be treated; second, this tube may be broken and its contents carefully dissolved in a solution of distilled water

to which a small amount of hydrochloric acid has been added, and each day the emanation is pumped by a mercury vacuum pump and compressed into minute capsules which may be applied to the surface which is to be radiated. As to the therapeutic action of either method, our results are the same; but with a large amount of radium it is safer to use the emanation method, since the tubes are apt to be lost through carelessness or they may explode and cause the loss of the radium.

We are employing in this hospital the small tubes of radium, and for protection against their possible explosion we have devised a permanent protector of brass 1 millimeter in thickness. This tube contains radium bromid salt and, as I have shown you, this radium in equilibrium is constantly emitting the Alpha, Beta, and Gamma rays; these rays are being thrown out continually in all directions.

The Alpha ray is a particle of matter about one-fourth the size of a hydrogen atom, and it is discharged from the mass with a velocity one-tenth that of light. These particles are positively charged, and it is said that 1 milligram of radium gives off 136,000,000 Alpha particles in a second. These particles can be shown by a small instrument called a "spinthariscope," constructed from a lens and a screen of zinc sulphid to which a small amount of radium has been added. It may be of interest to you to know that this combination of zinc sulphid and radium, used on luminous watches, was of great assistance in the recent war. All sorts of instruments and guns were equipped with this material, and owing to this Alpha bombardment they were made luminous. Our torpedo boats and airplanes were also equipped with this same material, thus avoiding the use of lights which would have proved dangerous by allowing the enemy to detect them. The Alpha rays have very feeble powers of penetration, so slight in fact that they have not the power to penetrate the glass of this tube.

The Beta ray is a small particle charged with negative electricity, moving at about the velocity of light. These rays are subdivided into soft and hard rays. The soft rays are very irritating to the skin, and their power of penetration is absorbed by

applying this screen of lead, 3 millimeters in thickness. These rays are useful in all superficial conditions.

The Gamma ray is described as a pulsation of ether having an extremely short wave length. These pulsations have tremendous powers of penetration, and it is necessary to use many inches of lead to completely absorb the rays. It is this ray that interests us particularly in the treatment of growths below the surface.

THE PHYSIOLOGIC ACTION OF RADIUM

What do these rays do? How do they affect disease?

If we place radium in a bottle of water we know that the water in a given time, owing to the action of the rays, will become disintegrated into its component parts, H and O. Whether the action of these rays on cell life is due to their ionizing power or their de-electrolizing power, we do not know; but we do know that penetrating through tissue cells they cause certain changes, the first of which is a swelling of the entire cell. The nucleus is seen to enlarge, and finally the cell becomes a colloidal mass capable of being absorbed by the blood-supply. The clearest description of the effects following the application of radium has been given by Ewing in the Journal of the American Medical Association, April 28, 1917, which I wish to quote to you in its entirety. In the material gathered in a series of uterine cases at different intervals—two of them having the organ removed two weeks after treatment—the following changes leading to the disappearance of the cervix may be traced: "Within three to five days after the application in the cervical canal of 300 mm. of radium emanation in a platinum tube, there is hyperemia of the tissues, beginning exudation of lymphocytes and polymorphonuclear leukocytes, and *swelling* of all the cells. In the second week, the cords of tumor cells present a characteristic appearance. The nuclei are swollen, homogeneous, and hyperchromatic, the cells loosened, hydropic vacuoles appear in the cytoplasm, and fusion giant cells form. In the third week, the number of cells is greatly reduced. Many appear to suffer liquefaction necrosis; others are invaded and mechanically broken

up or compressed by lymphocytes and proliferating stroma. From the fourth to the fifth weeks, only pyknotic nuclear fragments or an occasional giant cell are visible, or no traces whatever remain. Meantime, the stroma has been active and appears to take an important part in the process. Leukocytes become overabundant, the capillaries proliferate actively, and the stroma is transformed into granulation tissue in which numerous new capillaries penetrate and excavate the tumor cell nests. The gathering of leukocytes, lymphocytes, plasma cells, and polyblasts in the later stages of radium reaction may be extremely profuse, and in this respect the reaction is somewhat specific. Eventually the site of the tumor is occupied by granulation tissue from which slight serous and cellular exudate is discharged. Later, epithelium grows over the denuded surface, completing the repair. All manner of variations occur in the reaction of tumor tissue to radium. Complete simple necrosis follows overaction of radium. Bulky tumors may present large areas of simple necrosis in which cysts form by liquefaction. The stroma as well as the tissue is destroyed, in which event extensive scarring will result."

In the foregoing scheme of changes it would appear that just enough radium had been employed to cause slow degeneration of tumor cells and stimulate regenerative growth of granulation tissue.

It seems to me—and I am endeavoring to teach this subject from the standpoint of the effect of radium on cell life—that the fact of radium having the power to change cells into this colloidal state capable of being absorbed by the blood-supply clearly points to us the place that radium should occupy in therapy, particularly as to the treatment of malignant growths. Surgery is in many instances capable of removing the malignant mass, and its failure to establish a cure is due in the majority of cases to metastasis. Therefore it is our desire in this hospital to treat all growths before operation, thereby destroying the reproductive power of the cell. A cell incapable of regeneration cannot cause metastasis. Our method of treatment, then, is to give the malignant mass a thorough radiation, and

then, after three or possibly six weeks, remove the growth. As an additional safeguard after the operation we give radiation along the course of the scar, and all the surrounding tissue and lymphatic chains for a period of three months. The results in the past have proved to be very encouraging, and we hope in due course of time to standardize this method of treatment.

I want to say a few words as to a condition always present to a more or less degree in a patient receiving radium treatment. This condition I will speak of as a radium toxemia. The symptoms are as follows: There may be a rise in the temperature, or merely a feeling of prostration; the blood-pressure may be lowered; the pulse may be increased in frequency and sometimes a marked tachycardia is present; nausea and vomiting may occur, and very frequently the effect is such that our treatment must be temporarily discontinued. It is so necessary to combat this toxemia that I will read the standing orders for all radium cases before treatment.

(1) Urinary examination; if specific gravity is low, albumin or casts present, phenolsulphonephthalein test and blood chemistry.
(2) Complete blood examination, consisting of counts, red, white, hemoglobin, and differential.
(3) Blood-pressure taken before, during, and after treatment.
(4) Complete physical examination.
(5) Pathologic specimen to be taken for laboratory report.

The standing orders for all radium cases during treatment are:

(1) Pulse taken at least every hour.
(2) Blood-pressure if pulse is increased in frequency.
(3) Sodium bicarbonate, dram 1, to water 8 ounces, every three hours, with plenty of fluids otherwise.
(4) Hypodermically, arsenate of iron, gr. 1, strychnin $\frac{1}{60}$ gr., each day.
(5) Colonic irrigations: at least 4 quarts of sodium bicarbonate solution, dram 1 to 1 pint of water, each day.
(6) Diet as per individual.

A word as to the prognosis of these cases. The removal of the growth by the action of the radium rays depends entirely

upon its accessibility. If we have a growth that is superficially easy to ray on all sides, and the patient's physical condition is good, we can judge our prognosis from this standpoint.

The first series of cases that I will show today will be 3 cases of vernal or spring catarrh. This condition consists of a series of flat granules which appear on the under surface of both lids. These cases have been sent here from the New York Eye and Ear Infirmary, referred by Dr. Lewis A. Callan. This condition is to be differentiated from trachoma:

Vernal Catarrh.	*Trachoma.*
Conjunctiva of tarsus covered with broad flat papillæ, over which lies a bluish-white film. Do not ulcerate.	Conjunctiva of tarsus and culdesac covered with round hard trachoma bodies, with no pavement appearance. Tarsus greatly thickened. May ulcerate.
Papillæ persist during winter, but subjective symptoms subside.	No amelioration of any symptoms with change of seasons.
Cornea not often affected.	Cornea usually affected. Pannus.

I am told that the only successful treatment for this condition is radium.

CASE I.—The first patient, H. G., has been suffering from vernal catarrh for three years. He has had numerous treatments, consisting of various applications and curetments of the lids, but each time it has returned worse than before. He has had 35 mg. of radium applied to each eyelid for half an hour. The screenage has been $1\frac{1}{2}$ mm. of brass and 3 mm. of rubber. This tube has been applied directly to the surface after, however, we have thoroughly protected the eye with a piece of lead 4 mm. thick and at least 3 mm. of ordinary gauze.

His condition has improved, as you see; it may be necessary to give him only one more treatment.

CASE II.—The second patient, N. F., has been suffering from vernal catarrh for three years. This boy has received one treatment and his eyelids are practically normal. At first it was impossible for him to stand any light due to the concomitant photophobia.

CASE III.—The next patient, M. P., has had vernal catarrh for a period of two years. He has had two applications of radium and, as you see, the lids are in a comparatively normal state, all granules having disappeared. Judging from his previous condition he may be pronounced cured at this time.

CASE IV.—S. R., aged twenty-seven, referred by Dr. J. F. Erdmann with a diagnosis of carcinoma of the tongue. He came to the hospital on August 26, 1919, complaining of pain on the left side of his tongue over a period of seven months.

Family History.—Father and brother both alive and well. No history of tuberculosis or cancer in the family.

Past History.—He had influenza in October, 1918; no other illness; denies venereal history.

Present Condition.—In January, 1919, the patient first noticed a hard painful area on the left side of his tongue. He used a mouth-wash, but received no benefit. A month later a physician in Memphis, Tenn., cauterized this indurated area. As is always the history after cauterization, the lump became larger and the pain more severe, and since that time he has been rapidly growing worse. His physical condition reveals little aside from the condition of his tongue. As to the latter, the left half is thickened on the outer side. As you see, there is an ulcer about $\frac{1}{4}$ by $1\frac{1}{2}$ inches in size. The rest of the tongue is not hard to the touch, although very painful to palpation. Opposite to the ulcer, the last molar tooth is inclined inward so as to constantly irritate this ulcer. The glands of the neck are not enlarged.

In the treatment of this case our idea has been that he will receive radium applied directly to the ulcer until sufficient effect on the growth has been apparent; and then he will be referred to the surgical division where as much of the tongue will be removed as the surgeon thinks necessary. Dr. Robert Abbe reports 2 cases treated with radium before operation which are still alive at the end of fifteen years.

On September 11, 1919, this patient received 35 mg. of radium screened by 1 mm. of brass, 1 mm. of lead, and 3 mm. of

rubber. This was applied for two hours. After this treatment the pain was very much relieved and he had comparative comfort until three days ago (October 3d). He has returned now for further treatment, and will receive the same dosage and the same time of application.

The growth has taken on a decided softening, and his general physical condition is greatly improved. I think that after the treatment today we will be able in the course of two weeks to return this case to the surgical division for operation.

CASE V.—This man, M. A., aged fifty-five, was referred from the surgical division, with a diagnosis of carcinoma of the rectum. His chief complaint on coming to the hospital was pain in rectum for a duration of two months. The family history is entirely negative.

Past History.—Has always been in good health; no evidence of ever having had any cardiorespiratory or gastro-intestinal derangement; venereal history denied. About twenty years ago patient had pain in the lumbar region following severe physical effort. The physician attending him called it a "muscular strain." At the same time he had some bleeding from his rectum after defecation. This was attributed to a hemorrhoidal condition. About a year ago he had some bleeding from his rectum, and felt a mass protrude after stools. His physician sent him to a hospital where the mass was removed and he was advised that he needed a more extensive operation to get rid of the rest of the growth; but he improved so much after the operation that he neglected to follow this advice.

Present Illness.—For the past two months he has had persistant bloody mucoid discharge. He has a moderate amount of pain and has lost much blood. The surgical condition shows the anal margin stenosed. About 1½ inches above the anal margin is felt a mass which completely encircles the canal. This bleeds on the slightest irritation.

This man was first treated on August 1, 1919, with 35 mg. of radium screened by 1½ mm. of brass and 3 mm. of lead surrounded by 3 mm. of rubber, for twelve hours. He has had

three treatments in all, and today I assure you he is a greatly improved man. At the last clinic at least twelve of the class were able to examine this mass, by rectal palpation, and even under those circumstances it was impossible to find any evidence of bleeding. The mass, as you may note by feeling it, is confined to the lower angle of the rectum, and is a soft and fairly movable mass which the surgeon can remove with comparative ease. I would suggest that this man have at least one more treatment with radium, and I think we may promise very little likelihood of metastasis. The general condition has greatly improved. He complains of very little pain and has no hemorrhage. I have even suggested that it is possible for him to do light work.

CASE VI.—The next patient, H. L., twenty-seven years of age, is a man whom I treated at Camp Dix before my discharge from the army. This case was sent from the Walter Reed Hospital, with a diagnosis of Hodgkin's disease. The history was that eighteen months previously he noticed an enlargement of the left side of his neck which rapidly grew worse, and last January one of the glands was removed from his supraclavicular fossa and the diagnosis of Hodgkin's disease was made. At Camp Dix he received 300 mg. of radium with a screenage of 3 mm. of lead, applied over 1 inch of ordinary toweling, in three successive treatments of ten hours each. Marked improvement resulted, and he was discharged from the army and returned to his home in Boston. Last week he returned to New York for further treatment, and it was discovered that a few enlarged glands still exist in locations which had not been treated with radium. The general appearance is one of tremendous improvement. He has gained in weight, and unless we note very carefully both sides of the neck appear symmetric. He came into the hospital last week and was treated with 100 mg. of radium over eight different areas for a period of thirty hours. He says today that he feels much improved, but it may be necessary to give him further treatment within the course of a month.

CASE VII.—This patient is a baby, J. M., eight months old, with a congenital angioma. The history is that at birth there was a hard raised patch, about the size of a dollar, back of the ear. This increased in size and became more swollen until it was a mass 6½ inches in length and 5 inches in breadth. On September 29th this child had 35 mg. of radium applied below the hair margin and directly over growth with a screenage of 1½ mm. of brass and 3 mm. of rubber. Where this growth has been treated it shows decided improvement, and the growth below the hair-line shows evidences of shrinkage.

CASE VIII.—The next patient, Baby R., aged two months, has a congenital angioma of the upper lip. This condition has been treated with various caustics and has become infected. There was a constant tendency to bleed, and the poor baby showed marked evidences of the previous treatment. On September 29, 1919, one dose of 35 mg. of radium protected by 1½ millimeters of brass and 3 mm. of rubber was applied for one hour. The growth shows marked diminution in size and the baby has had no bleeding since the application. It is hoped that only one more treatment will be required to restore this lip to its normal contour.

CASE IX.—This patient, R., a colored woman aged forty-six, noticed in February of this year a lump in her breast about the size of a marble. This rapidly increased in size and hardness until at the present time the breast cannot be moved. On physical examination we found the right breast very large, infiltrated, and very hard, the infiltration extending to the median line upward to the clavicle and posteriorly to the post-axillary line. Everywhere throughout there is a board-like hardness. The axillary and cervical nodes on the right side are large and hard. The patient is unable to move her right arm.

She was admitted to the hospital on September 10th. This mass was divided into three circular zones, and each zone was subdivided into a space 1½ inches square. These spaces were

treated for six hours with 100 mg. of radium protected by 3 mm. of lead, 3 mm. of rubber, and 1 inch of toweling. Today you see the breast is much softer; two carcinomatous nodules that appeared at the upper margin of the mass have disappeared. The breast is much softer and smaller, and she is able to move her arm with comparative freedom. Today this same treatment will be repeated.

What may we expect in a case that has advanced to this stage? Nothing can be done for it surgically, and our only hope is radium. I will show this patient to the class every two or three weeks.

I may add that her physical improvement has been very marked.

CASE X.—This man, J. C., aged sixty-one, has come from Georgia, complaining of a tumor on the left side of his neck, which has been there since January.

Family History.—His father is living at the age of eighty-two, and has "cancer of the face." The patient's health has always been good.

Present History.—Last January he noted a slight swelling on the left side of the neck. This grew larger until March, when it was about the size of a walnut. He then went to a physician, who operated and opened the growth. In April the growth rapidly began to enlarge, and he has noted no general improvement in his health since the operation. This growth has been diagnosed as a lymphosarcoma, although as yet we have not received the pathologic report. The mass is the size of a large apple, immovable, and has a sinus 1 inch in diameter, which is constantly discharging a vile-smelling fluid.

This mass was divided into six squares, and 107 mg. of radium, with 3 mm. of lead screenage plus 3 mm. of rubber, radiated through $\frac{3}{4}$ inch of toweling. Each space was treated for six hours. He had very little reaction, although his temperature last night was above normal. Radium in lymphosarcoma has always given remarkable results, and I do not hesitate to promise that within six weeks this growth will have been entirely re-

moved. However, I will show him to you at each clinic and have you watch him with me.

CASE XI.—This man, J. L. M., aged thirty-four, was referred by Dr. Erdmann, with a diagnosis of carcinoma of the rectum. About six months ago he noticed pain immediately following defecation. He has had some bleeding. Examination shows a growth involving the lateral right rectal wall about 2 inches long and 1 inch wide. Two weeks ago today he was treated with 100 mg. of radium, screened with 3 mm. of lead and 3 mm. of rubber. Today he tells us that he has been practically free from pain and his general condition is much improved. The growth is soft and more movable, and the same treatment will be repeated today. I expect to show him to you again two weeks from today.

The next two cases will demonstrate the postoperative treatment of malignant growths with radium.

CASE XII.—F. K., aged fifty, has for many years been a sufferer with what was termed a chronic type of indigestion. Two years ago his physician diagnosed the trouble as a gastric ulcer and advised an operation. This was put off and he did not consult a physician until last June. At that time the symptoms had grown very much worse, and, due to his gastric retention, immediate operation was advised.

He was operated upon by Dr. Charles Gordon Heyd on July 10, 1919. Dr. Heyd definitely stated that a few glands remained which it was impossible to remove.

He received his first radium treatment on August 4th. This consisted of five and a half hours' treatment over the squares 1 inch in diameter that had been mapped out by Dr. Heyd; 100 mg. were used on each square. He received another treatment for five and a half hours over another area on August 11th. On the 20th he was treated again for five hours with 100 mg. over each square. Since that time he has received seven more hours of treatment of 100 mg., and today reports an increase of 21 pounds in weight. He has received tremendous relief, and we

feel that with occasional treatments the improvement will continue.

CASE XIII.—J. D., aged thirty-seven, policeman. His chief complaint on admission was "pain" in his stomach extending over a period of eight months. Childhood history negative. Four years ago he had an operation for appendicitis, and at the same time a gastro-enterostomy was done. Since then his condition has not improved, and he came to the hospital on September 5th. He vomits about two hours after meals and has a great deal of pain. The vomitus is yellow and watery, about a pint in amount, and he states that it tastes like coffee.

He was operated on the 23d of last month by Dr. Heyd, who reported an inoperable carcinoma involving the pylorus and duodenum. The mass is fixed and many glands are impaired in all directions.

As a last resort, the case was turned over to our radium service, and to date we have given him one treatment consisting of the radiation of eight squares above the tumor mass, each square being radiated with 100 mg. of radium for six hours. At the present time his condition seems better, and we can at least promise him some relief from the constant pain that always accompanies these cases.

CLINIC OF DRS. M. A. ROTHSCHILD AND A. O. WILENSKY

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CHOLELITHIASIS

General Theory of Cholesterol Metabolism as Related to Gall-stones. Value of Blood Examination for Cholesterin as a Diagnostic Aid. Interpretation of Individual Clinical Pictures in Order to Be Able to Select Cases in the Diathetic Group. Rational Postoperative Treatment in Cases of Last Group, in Order to Prevent Recurrence of Symptoms and the Performance of Unnecessary Operations.

IT is our purpose to illustrate by a series of cases the relationship of the cholesterol metabolism to the formation of calculi in the biliary tract. Hitherto the infectious theory of the formation of biliary stones has been emphasized too greatly and has practically dominated medicine. Since 1909, however, it has begun to be displaced by a new conception introduced by Aschoff and Badmeister—that the abnormalities in the cholesterol metabolism play an important part in the formation of gall-stones. An abundance of proof has subsequently been furnished of the close interrelationship existing between the formation of biliary stones and the cholesterol metabolism.

It has been definitely shown that hypercholesterinemia predisposes to gall-stone formation for the following reasons: (1) Races whose blood is poor in cholesterin rarely have gall-stones; (2) those races whose blood is richer in cholesterin very frequently have gall-stones; (3) in states in which a physiologic hypercholesterinemia occurs, such as in pregnancy, stones are most commonly formed.

In the cases of groups one and two the cholesterol content of the blood seems to depend on the cholesterol content of the customary food of the people. This observation has been confirmed in a number of experiments, because it is possible to produce in animals a hypercholesterinemia by feeding an excess of cholesterol bodies in the food, and even to produce small concrements in the gall-bladder.

The prevalent theory of the cholesterol metabolism is that the cholesterol bodies are normally derived to the greatest extent from the cholesterol content of the food; that the latter is absorbed from the intestinal tract; and that it is an excretory product of the liver through the bile.

In the formation of stones, the cholesterol content of the bile is most important. The bile may be considered as a colloidal solution. Such a solution is subject to the ordinary physical and chemical laws, and precipitations may follow a supersaturation of any of the ingredients or a disturbance of the normal equilibrium. It is our purpose to emphasize that in hypercholesterinemic states the bile may become supersaturated and true precipitation of stones may result. This is shown by the fact that stones containing practically 100 per cent. cholesterol are very common; these are practically always bacteriologically sterile, and the gall-bladder shows little or no pathologico-anatomic change. However, it frequently happens that secondary infection takes place, and that the manifestations of the latter completely hide the underlying metabolic disturbance.

The precipitation of cholesterol in the form of stones in the gall-bladder may result in the reduction to the relative normal[1] of any hypercholesterinemia. It follows immediately, therefore, that the diagnostic value of any blood determination is unreliable as indicating the presence of stones in some part of the biliary tract, because a hypercholesterinemia may exist before stones are precipitated out; whereas a second examination may show a normal cholesterol content of the blood after the precipitation of stones in some portion of the biliary tract.

[1] The cholesterol content of the blood of normal persons varies from 120 to 180 mg. per 100 c.c. of blood. The cholesterol content of normal bile varies from 0.4 to 0.7 per 100 c.c. of bile.

In addition, other factors which influence the cholesterol metabolism are very common, such as febrile conditions which reduce the cholesterinemia, and atherosclerosis, diabetes, inanition, or nephritis, which may increase the cholesterinemia.

In cholelithiasis accompanied with common duct obstruction, hypercholesterinemia is almost invariable. This has led us to divide our investigations into two groups, with subgroups, as indicated in the subjoined table:

I. Cases with a normal cholesterol content of the blood.
II. Cases of hypercholesterinemia:
  (*a*) Obstructive
    Permanent,
    Temporary
      Stone.
      Stricture.
      New growth, etc.
  (*b*) Diathetic
    With obstruction,
    Without obstruction
      Intermittent.
      Permanent.

The following cases illustrate these principles:

CASE I.—This thirty-three-year-old woman, a housewife, has for the last year and a half had frequent attacks of abdominal cramps associated with vomiting. No jaundice has ever been noticed. The physical examination, with the exception of some tenderness in the right iliac fossa, is negative. There is no nephritis present.

The patient was explored and the operation revealed a normal looking gall-bladder which contained a single fairly large stone. An ideal cholecystotomy was done and the single stone was removed. At the same time an appendicectomy was done. The patient recovered from the operation; there were no postoperative complications, and she was discharged from the hospital feeling perfectly well. Before the operation examination of the blood showed that the latter contained 0.1825 gm. of cholesterol per 100 c.c. of blood.

The essential parts of this history are that the patient had a practically normal gall-bladder containing a single stone, which chemical examination showed to be almost entirely composed of

cholesterol; and that the cholesterol content of the blood was well within normal limits. In the first place, we have a patient in whom the cholesterol examination of the blood yielded no help in a diagnostic way. The explanation for this state of affairs is that at some time previous to the operation—possibly during a pregnancy—the patient had passed through a period in which a hypercholesterinemia was present. The latter abnormality was reduced to the normal by a precipitation of the excess of cholesterol and the resultant formation of the single large cholesterol stone. Subsequent to this the patient had symptoms referable to the stone acting as a foreign body, and because of these manifestations the operation was performed. At the time of operation the blood findings demonstrated that the condition of the cholesterol metabolism, as reflected in the blood-picture, was normal.

CASE II.—This twenty-four-year-old woman is a housewife, and has had attacks of gall-bladder colic for the last seven and a half years, and with increasing frequency. The physical examination of the patient was negative. At the operation a practically normal gall-bladder was found which proved to contain a large number of stones. Some of the latter contained a preponderance of cholesterol; others had nuclei of cholesterol and outer coatings of biliary pigment. The blood examination taken before operation showed that the blood contained 0.1725 gm. of cholesterol per 100 c.c. of blood.

This case is very similar to the first. Again we have a condition in which pre-existing states of hypercholesterinemia had been reduced to the normal by a precipitation of stones in the gall-bladder; acting as nuclei, these calculi had abstracted from the bile some of the bile pigment. The abnormal hypercholesterinemic states had completely disappeared, or the patient was in a temporarily normal condition at the time of the operation; and the cholesterol metabolism, as indicated by the blood examination, was in a normal state.

CASE III.—This forty-three-year-old woman has had two attacks of sharp pain in the right upper abdominal quadrant—

the first attack four weeks ago and the second attack five days ago. At no time was there any jaundice. The physical examination disclosed some emphysema, some hypertrophy of the heart, a palpable liver, and a palpably enlarged gall-bladder. The temperature was 101° F. At operation a large distended gall-bladder was found, the contents of which included bile and pus intimately mixed and a number of stones. Cholecystectomy was done, but no drainage of bile was instituted. Before operation examination of the blood showed 0.155 gm. of cholesterol per 100 c.c. of blood.

This case is similar to the second case, with the exception that a complication has been added. Essentially the same conditions prevail—that is, at some time preceding the operation one or more states of hypercholesterinemia had existed which had been reduced to the normal by a precipitation of stones. These apparently had lain quiescent in the gall-bladder for an unknown length of time until four weeks previous to admission, when an infection had taken place and an empyema of the gall-bladder had resulted.

Two points are illustrated by this case. In the first place, at the time of operation a hypercholesterinemic state did not exist, and the symptoms for which the patient sought treatment were not due to the stones except as they aided in inviting the infection. Second, the presence of any febrile condition can by itself reduce the quantity of cholesterol in the blood. We have no means of telling whether if the febrile condition had not existed the figure for the blood determination might not have been higher and have indicated a hypercholesterinemic state. Some of the stones in the gall-bladder had a good deal of bile pigment. This was probably due to a secondary layering over a cholesterol core, or to the fact that the infection caused the formation of secondary mixed stones.

CASE IV.—This woman is thirty years old and since three weeks before she was admitted to the hospital she has had attacks of epigastric pain, each of which lasted from a few minutes to half an hour. At no time has she been jaundiced. Except for

some tenderness in the general region of the gall-bladder the physical examination disclosed nothing abnormal. At the operation the gall-bladder was found to be not inflamed, but to contain a great many gall-stones, most of which had a cholesterol nucleus and an outer coating of biliary pigment. Examination of the blood before operation showed a content of cholesterol of 0.215 gm. per 100 c.c. of blood.

In this patient we have evidence of the continuation of the process which originally had incited a precipitation of stones. At the time of the examination the blood showed the presence of a hypercholesterinemic state. The number of stones found in the gall-bladder and their physical characteristics indicate the probability that the hypercholesterinemic state pre-existed for a long time either continuously or possibly—and perhaps more probably—there had been a number of periods in the patient's life in which a hypercholesterinemic state had existed, separated by other periods in which the cholesterol metabolism was relatively normal. The precipitation of stones might have occurred at the end of, and might have been the cause for, the termination of each one of the periods of hypercholesterinemia; or the deposition might have occurred intermittently when the abnormal state was a continouous one, in which case the deposition of the concrements merely served to remove only a part of the excess of cholesterol. In either case the process is evidently a purely diathetic one.

A cholecystostomy was done. We present a table indicating the changes in the cholesterol metabolism:

	Blood,	Bile:			Urine,	Stool,
	per cent.	C.c.	Sp. gr.	Per cent.	bile.	clay col.
July 31	0.215					
August 1	.....	336	1010	0.0575	No	No
" 2	.....	96	1010	0.0375	"	"
" 3	.....	80	1010	0.0945	"	"
" 4	.....	170	1008	0.0325	"	"
" 5	0.140	100	1010	0.069	"	"
" 7	.....	194	1008	0.0685	"	"
" 9	.....	352	1001	0.100	"	"
" 17	0.1625				"	"

With the discharge of bile from the biliary fistula the blood content of cholesterol gradually fell, until five days later the content measured 0.140 gm. per 100 c.c. of blood. At the time of the discharge from the hospital this had risen again to 0.1625 gm. per 100 c.c. of blood. Such a depletion of the cholesterol content of the blood follows adequate biliary drainage, inasmuch as little or no bile reaches the intestine under these conditions and inasmuch as the intestinal tract forms one of the main sources whence the normal content of bile is maintained. We shall see later that when the drainage occurs from the common bile-duct this depletion can reach an extreme grade, because when the drainage is instituted only into the gall-bladder a considerable proportion of bile escapes down the common and hepatic bile-ducts into the duodenum.

A number of other factors are also present in this case, all of which have a tendency toward reducing the amount of cholesterol in the blood-stream, namely: the patient has been through an operation, which is usually accompanied by a febrile period; and during this period the lipoid content of the food is at a minimum. That all of these factors are only temporary and that subsequently a hypercholesterinemic state may return is shown by the fact that within a month after the patient was discharged from the hospital a hypercholesterinemic state was again present, as shown by the examination of the blood.

One of the complicating factors with which one has constantly to deal is the presence of obstruction in any one of the ducts of the biliary system. The following cases will illustrate the presence of obstruction in the cystic and in the common duct:

CASE V.—A forty-year-old patient, a woman, has had attacks of abdominal pain for two months. At no time previous to her admission to the hospital was she jaundiced. Physical examination, however, disclosed a subicteric tint to the conjunctiva, a large liver, and a large gall-bladder. At the operation there was a pure hydrops of the gall-bladder, and a single stone was found wedged in the cystic duct. The blood examination before the operation showed 0.235 gm. of cholesterol per 100 c.c. of blood.

The presence of the slight icterus immediately shows that a relative obstruction is present in the common duct, and we know from our experiences that the presence of obstruction always causes a hypercholesterinemia. It is not necessary that the obstruction in the common duct be due to a stone; the obstruction may be due to the presence of inflammatory thickening and swelling of the duct wall, or to the presence of some extraneous mass pressing upon it, or to the presence of a tumor growing within it.

In this patient, as in all cases in which a stone is wedged in the cystic duct, a great deal of inflammatory swelling was present in the tissues. Some of this always implicates the adjacent common duct structures. Necessarily, that must account for the high cholesterol figure of the blood examination. Otherwise, as one can see from the case previously cited, the conditions here are probably identical with those in Case I in so far as any diathetic element is concerned. The single cholesterol stone indicates that at some previous time a hypercholesterinemia had been reduced to the normal. The hydrops for which the patient was operated upon is due to the mechanical obstruction to the outflow of the gall-bladder contents by the impaction of the stone in the cystic duct. The high figure in the blood should therefore reflect the complicating factor, namely, the obstructive jaundice.

CASE VI.—Our next patient is a woman of fifty-six, who came to the hospital after her first attack of abdominal pain. The attack was very severe, and during the last day or two some jaundice has been apparent in the skin and in the conjunctiva. So far as the patient knows, the stools are normal in color. The physical examination showed a palpable gall-bladder; and that part of the abdominal wall overlying it was rigid and tender. She was markedly jaundiced at the time of the examination. The urine contained a large amount of bile, and the stools were clay colored.

At operation an empyema of the gall-bladder was found associated with much pericholecystitis and with a pericholecystitic abscess, and a large stone was found blocking the common duct.

A cholecystectomy was done. The common duct was drained with a large rubber tube. No nephritis was present at any time, either before or after operation. The jaundice quickly subsided and the patient made a complete recovery.

The disturbances in the cholesterol metabolism are indicated in the table:

1915.		Blood, per cent.	Bile: C.c.	Sp. gr.	Per cent.	Urine, bile.	Stool, clay col.
June	22.....	0.237					
"	25.....	.....	270	.....	0.140	No.	Yes
"	26.....	.....	130	.....	0.136	"	"
"	27.....	.....	130	.....	0.085	"	"
"	28.....	0.137	245	.....	0.106	"	"
"	29.....	.....	220	.....	0.120	"	"
"	30.....	.....	160	.....	0.115	"	"
July	1.....	.....	320	.....	0.115	"	"
"	2.....	.....	240	.....	0.118	"	"
"	20.....	0.147					
August	29.....	0.272					
September	19 put on diet.						
October	3 Blood, 0.185 per cent.; temperature normal.						

Before operation a hypercholesterinemia was present. We have no means of telling before operation just what this indicates in a case of this kind. We are confronted by a patient with a common duct obstruction and we know from our experiences that a hypercholesterinemia can be due to the common duct obstruction alone. We have no means of telling, however, how much of the hypercholesterinemia is due to the common duct obstruction or how much of it is due to an underlying diathesis, the manifestation of which may be present at the time the examination is made. To form a correct judgment, information is necessary as to the exact anatomic conditions present and as to the subsequent behavior of the cholesterol metabolism as reflected in repeated blood examinations. In this particular patient the immediate effect of the operation and the common duct drainage yielded a disappearance of the jaundice and a marked depletion of the cholesterol content of the blood. This state of affairs continued until the patient's discharge from the hospital, at which time the condition of the cholesterol metabolism was apparently normal, as indicated by the blood examination, which showed a

content of 0.147 gm. per 100 c.c. of blood. If we had never seen this patient again we could have assumed that the entire abnormality of the cholesterol metabolism was due to the obstruction; but subsequently we were fortunate enough to be able to follow her, and later we found that the hypercholesterinemia returned, as shown by repeated examinations of the blood.

To illustrate this point more completely, we show the next case.

CASE VII.—This woman in the last four months has had repeated attacks of right abdominal pain, with vomiting, jaundice, and clay-colored stools. At the operation stones were found in a much contracted and acutely inflamed gall-bladder, and in the dilated common duct many stones were found in addition; much pericholecystitis was also present. Essentially the anatomic conditions were the exact replica of those in the preceding case, and before operation the blood content of cholesterol was also high. Essentially the same course of affairs followed during the convalescence, and at the discharge of the patient from the hospital the cholesterol metabolism was in normal condition.

The same line of reasoning is made in this case as in the preceding. We were not able to tell before operation how much of the hypercholesterinemia was due to the common duct obstruction and how much to an underlying diathesis, and unless the subsequent course of events is accompanied with a return of the hypercholesterinemia we cannot assume that any disturbance of metabolism exists. In this patient a number of examinations subsequent to operation showed no variation from the relatively normal figures of the cholesterol metabolism, and we assume, then, that the hypercholesterinemia present before operation was entirely due to the presence of the common duct obstruction.

It is very important to understand the effect of bile drainage upon the cholesterol metabolism, as is illustrated by these cases.

CASES VIII and IX are both women between forty and fifty years old in whom attacks of cholecystitis with jaundice had occurred during the past year and a half. A cholecystostomy

was done in both cases, and in both patients thin-walled, distended, and inflamed gall-bladders were found containing numerous stones. The two following tables indicate the course of affairs in the cholesterol metabolism of both these patients:

CASE VIII

Date.	Blood cholesterin mg. per cent.	Bile cholesterin mg. per cent.	Biliuria.	Stool.
Preoperative:				
May 28	0.2725			
June 2	0.250			
Postoperative:				
June 4	.....	0.100	None	Colored
" 5	.....	0.100	"	"
" 6	.....	0.075	"	"
" 7	.....	0.067	"	"
" 8	.....	0.134	"	"
" 10	.....	0.120	"	"
" 11	0.16675	0.108	"	"
" 12	.....	0.102	"	"
" 13	.....	0.092	"	"
" 15	.....	0.089	"	"
" 16	.....	0.079	"	"

CASE IX

Date.	Blood cholesterin mg. per cent.	Bile cholesterin mg. per cent.	Biliuria.	Stool.
Preoperative:				
September 15	0.220			
Postoperative:				
September 24	.....	0.091	None	Acholic
" 25	0.1415	0.085	"	"
" 27	.....	0.0765	"	"
" 27	.....	0.125	"	"
" 28	.....	0.085	"	Colored
" 29	.....	0.110	"	"
" 30	.....	0.106	"	"
October 1	.....	0.0905	"	"
" 3	.....	0.094	"	"
" 5	.....	0.116	"	"
" 8	.....	0.0825	"	"
" 12	0.0837			

Case VIII had no obstruction in the common duct. Relatively small amounts of bile had escaped and the stools were well colored. The bile content of cholesterol was relatively well within normal limits, indicating that sufficient quantities of choles-

terol bodies were being reabsorbed from the intestinal tract to maintain the normal cholesterol content of the bile. Case No. IX, for some reason, had, immediately following the operation, some inflammatory obstruction in the common duct, as indicated by the clay-colored stools. There was no bile in the urine and no jaundice, because all the bile was escaping through the gall-bladder fistula. The cholesterol content of both blood and bile, and especially the content of the blood, fell far below the normal level, indicating that the body was being depleted of its cholesterol. In both of these cases the food factor was constant, both the patients being upon the same diet.

The effect of the drainage of bile from the common bile-duct is illustrated in the table given with Case No. VI. The effect is similar to that of gall-bladder drainage, except that it is carried to an extreme degree, and it corresponds most nearly with the effect observed in Case IX, in which a gall-bladder fistula is associated with a common duct obstruction.

The effects of these two means of bile drainage may be summarized as follows:

1. With common duct drainage the system is rapidly depleted of its cholesterol.

2. Gall-bladder drainage does not accomplish this extreme effect unless there be a concomitant obstruction in the common bile-duct.

3. The rate of drop varies and depends upon the initial figure and the length of time of the discharge. After a certain minimum is reached there is no further fall in the cholesterol content of the blood.

4. These effects are obtainable only when the operation has been so performed that proper bile drainage is accomplished and all obstructions have been removed from the ducts.

The loss of bile produced by a biliary fistula has a deleterious effect upon the animal body, and when this has lasted for an appreciable length of time the patients are liable to exhibit any or all of the following symptoms:

1. Disturbance of the digestive function, frequently accompanied by vomiting.

2. Greater or less degree of constipation, induced by an absence of bile from the intestinal tract.

3. Depreciation in the general well-being and vigor of the body and a deterioration in the patient's general condition, as evidenced by an impairment in the circulation, in a lessened resistance to bacterial or other trauma, and in a general lassitude and muscular weakness.

This deleterious effect may be counteracted or may be forestalled by collecting the biliary drainage and feeding it to the patient by stomach-tube. Occasionally one meets with a patient who is able to drink the bile directly, and for this type of patient some of the obnoxiousness may be removed by the addition of salt to the bile.

We give next a very remarkable case in which the variations of the cholesterol metabolism furnished very important data.

CASE X.—In a twenty-seven-year-old married woman three attacks of gall-stone colic had occurred four months, six weeks, and four days previous to admission to the hospital; the last two attacks were accompanied by slight degrees of jaundice. The patient was slightly jaundiced at the time of operation. At the operation (September 8th) a normal looking gall-bladder was found to contain small greenish-black stones, and the hepatic and common ducts were apparently empty. A cholecystostomy was done. The contents of the gall-bladder were sterile bacteriologically.

On September 12th there was an attack of colic, with slight icterus, which entirely subsided by September 17th. On September 26th the notes state that the discharge of bile from the fistula had been profuse, the fluid had been turbid and green in color, and a stone had been felt in the gall-bladder on the previous day. This was extracted on September 26th. Up to October 12th, however, the drainage had continued to be just as profuse, and on the day following the bile passages were explored. A secondary cholecystectomy was done, and a stone which was impacted in the papilla was extracted. The hepatic ducts were drained. The character of the bile drainage changed immedi-

ately and the color of the bile became clear golden yellow. The convalescence was uneventful thereafter. The cholesterol variations were indicated as follows:

Date.	Temp., Fahr.	Blood cholesterin mg. per cent.	Bile cholesterin			Biliuria.	Stool.
			Cc.	Sp. gr.	Mg. per cent.		
Preoperative:							
September 6	99.8°	0.155					
Postoperative:					(G. B.)		
September 8	100.0°	.....	...	....	0.117		
	101.2°	.....	190	1010	0.061	None	Acholic
" 10	100.4°	.....	140	1010	0.037	"	"
			70	1010	0.054	"	"
" 11	99.8°	.....	102	1010	0.0545	"	"
			88	1010	0.051	"	"
" 13	103.0°	.....	130	1010	0.0352	"	"
" 14	102.4°	.....	192	1010	0.022	"	"
" 15	100.2°	.....	122	....	0.0082	"	"
" 16	100.2°	0.162	270	1008	0.031	"	"
" 17	99.2°	.....	275	1010	0.0205	"	"
" 18	99.2°	.....	470	....	0.0355	"	"
" 28	101.4°	.....	450	1010	0.031	"	"
" 29	99.4°	.....	530	1010	0.044	Trace	"
October 1	99.0°	0.165	...	....	.....	None	"
" 14	101.8°	.....	111	1012	0.025	"	"
" 15	101.6°	.....	110	1010	0.0345	"	Sl. col.
" 17	99.8°	.....	...	....	0.066	"	Colored
" 21	99.6°	.....	...	....	0.0475	"	Well col
" 23	99.6°	.....	...	....	0.075	"	"
" 28	99.4°	0.125					

While studying this case we were impressed by the fact that the cholesterol content of the blood did not fall after operation to the level to which ordinarily we were accustomed to see it fall, and we suspected that the bile-passages were not absolutely free. It was only after the second operation, when the common bile-duct was cleared, that we saw the cholesterol content of the blood fall to the expected low level. In several instances occurring subsequently we made use of this principle in making the diagnosis that the ducts had not been thoroughly cleared, and were later much gratified to have our diagnosis verified.

One can make use of this principle as a criterion for determining the appropriate time when bile drainage should be discontinued; and in our experience we have found that this should be done as soon as the blood is found to contain a relatively normal amount of cholesterol. Practically, this usually coincides with relatively normal amounts of cholesterol in the bile and with a normally appearing bile, and not until the bile content of cholesterol does fall to relatively normal limits do these changes occur in the escaping bile.

In a number of cases the postoperative course has been found to include certain subjective complaints which have been accompanied by hypercholesterinemia. We have found that if such patients are put on a diet from which lipoid elements, such as fat, butter, yolk of egg, etc., are excluded, that improvements will occur in the subjective symptoms concomitantly with a reduction of the hypercholesterinemia to normal.

CASE XI illustrates this point. This woman, before her original operation, had a hypercholesterinemia. During her stay in the hospital this had been reduced by bile drainage, so that at the time of her discharge from the hospital the blood content of cholesterol was 0.130 gm. of cholesterol per 100 c.c. of blood. During the following year, as indicated in the subjoined table, there were periods when the subjective symptoms (mostly pain and distress in the right upper quadrant) were associated with a relative hypercholesterinemia.

1915		Symptoms.	Blood, per cent.	Temperature.
April	22	None	0.1625	
May	8	"	0.1875	
"	20	"		
June	4	"	0.155	
September	16	"	0.175	
November	4	"	0.1735	
1916				
February	9	"	0.150	
April	26	"	0.140	
May	26	Distention after meals; headache and dizziness. Menopause?	0.170	

The periods in which the chart indicates that the hypercholesterinemia was within normal limits were due to a restriction of the lipoid elements in the diet; and clinically these periods were associated with a comparative freedom from symptoms.

To summarize: We have attempted to emphasize the following important points:

1. The aseptic formation of biliary calculi occurs, and a special type of stone characterizes this condition.

2. Disturbances of cholesterol metabolism are intimately associated with the formation of these stones.

3. The cholesterol content of the blood *per se* cannot be used as a diagnostic criterion.

4. The cholesterol content of the blood taken in conjunction with the anatomic and pathologic findings is of great service in analyzing the individual case. This point is especially valuable in the after-treatment of those cases of so-called chronic cholelithiasis in which repeated operations are performed. By recognizing the diathetic element involved it is possible to keep this group free from symptoms for long periods.

5. In those cases of cholelithiasis with hypercholesterinemia in which no obstructive cause for the hypercholesterinemia can be found, adequate biliary drainage should be instituted.

6. The return of the cholesterol metabolism to the normal state, as determined by chemical examination of the blood and bile, gives the indication for the removal of the drainage-tube.

7. Cases belonging in this group should be followed up, and repeated examination of the cholesterol content of their blood made. If a case again becomes hypercholesterinemic, the patient should be put on a diet relatively free of fats and lipoids.

CLINIC OF DR. MORRIS H. KAHN

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THE FUNCTIONAL DIAGNOSIS OF THE HEART

The Tests of Heart Function. Irregularities of the Heart-beat. Variations in the Rate of the Heart-beat. Pulsus Alternans. Symptoms in Other Organs. Stasis in the Pulmonary Capillaries, Edema, and Other Phenomena. Auscultatory Signs. Tests Depending Upon Changes of Pulse-rate. Instrumental Studies of Heart Function. Blood-pressure Variations. Effect of Exercise on the Blood-pressure. Variation Tests. Technic of Tests. Polygraphic Tracings and Their Value in Functional Diagnosis. Electrocardiographic Changes Associated with Myocardial Involvement with Special Reference to Prognosis. Vital Capacity of the Lungs as a Test of Myocardial Function. The Myocardial Retraction Reflex. Myocardial Dilatation Reflex. The Elimination of Salt as an Index of Heart Function.

IT is the aim of functional diagnosis of the heart to estimate its functional integrity as a pump, to learn if the heart may submit to the usual demands of active life, and if it can undergo an anticipated amount of strain such as is entailed by anesthesia, childbirth, febrile toxemia, etc.

Functional diagnosis also serves as a clinical index of the increase or diminution of the heart's efficiency as the result of treatment or muscular work.

In a comprehensive study of circulatory efficiency, therefore, it should be our aim to ascertain which of the various portions of the cardiovascular mechanism are intact and which are deranged, to what extent the derangement of structure and function affects the circulation of the blood, and to what degree it affects the normal activity and the longevity of the individual.

The complementary action of the vasomotor system is very important in maintaining adequate circulation. This factor is different in different individuals, and its variations are perhaps the greatest source of error in determining the efficiency of the circulation.

THE RESERVE FORCE OF THE HEART

During its normal activity the heart possesses an available reserve force by means of which the amount of circulation may be increased. In a state of vasomotor incompetence, therefore, the task of transporting the oxygen and of increasing the velocity of the circulation devolves upon the cardiac motive power.

Changes in the circulation may be occasioned by nervous influences, vascular dilatation and contraction, and by alteration of the heart's action. The first two factors are very variable.

The reserve force of the heart may evince itself in two ways, *i. e.*, either by an increase in rate or by an increase in the systolic output with each beat. Different individuals react differently in this respect. In untrained hearts, as well as in the chronic infections and cachectic diseases and in states of nervous or psychic stimulation, the heart usually reacts by an increase in rate.

The increased rate if excessive may partly defeat its purpose. Complete and prolonged systolic contraction usually takes place at the expense of the diastolic period. The tachycardia may become so marked that the period of diastole will be shortened to such a degree that the filling of the ventricle will be very deficient. A small systolic output will naturally result. The *x*-ray in such an instance would show the size of the heart during diastole to be less than normal.

In athletes, on the other hand, or in cases in which exercise has been practised, the increased diastolic intake and systolic output make up for the circulatory need. In the latter case the heart dilates, increasing its capacity, so that with each contraction there ensues the expulsion of a larger quantity of blood into the systemic circulation.

Normally a small amount of residual blood remains in the heart even after complete contraction. If the diastolic intake is

abundant and the heart muscle is too weak to expel the entire contents with each systole an increasing amount of residual blood remains in the left ventricle after each heart-beat. The *x*-ray in this instance would show a heart dilated above normal during its diastolic phase.

THE TESTS OF HEART FUNCTION

Most of the tests of heart function are based upon circulatory changes produced by muscular exertion. The clinical symptoms and physical signs may indicate the direction, but probably not the exact level of cardiac efficiency. Changes of pulse-rate and blood-pressure reveal important criteria in the study of heart function. The technical methods, the sphygmograph and electrocardiograph, and the Roentgen ray have proved themselves valuable adjuvants.

A more or less complete analysis of heart function, therefore, should comprise: Certain clinical observations; tests depending upon changes of pulse-rate; those depending upon blood-pressure studies and blood-pressure variations; instrumental tests by means of the polygraph, electrocardiograph, and *x*-rays; and certain metabolic studies.

CLINICAL STUDIES OF HEART FUNCTION

1. Irregularities of the pulse.
2. Variations in the pulse-rate.
3. Pulsus alternans.
4. Auscultatory signs in testing heart function.
5. Evidence in other organs.

Irregularities of the Heart-beat.—Respiratory arhythmia and the "youthful irregularity" of Mackenzie do not indicate any disturbance of heart function. In fact, its presence indicates normal heart muscle (Fig. 78).

All other forms of arhythmia are not without significance. Irregular action implies a waste of the heart's energy. After a premature ventricular contraction there ensues a compensatory pause during which the ventricle is overfilled with blood. The following contraction is necessarily exaggerated in order to expel the increased content. When extrasystoles are frequent, as in

pulsus bigeminus or in pulsus trigeminus, abnormally large quantities of blood are mobilized with each normal systole. This may eventually lead to fatigue of the ventricular muscle (Fig. 79).

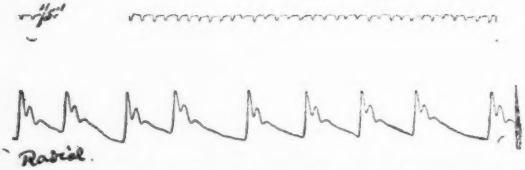

Fig. 78.—Tracing of the radial pulse showing normal sinus irregularity.

With the pulsus irregularis perpetuus, of auricular fibrillation, a great number of the heart's contractions are incomplete and are of little or no value to the circulation. The heart is

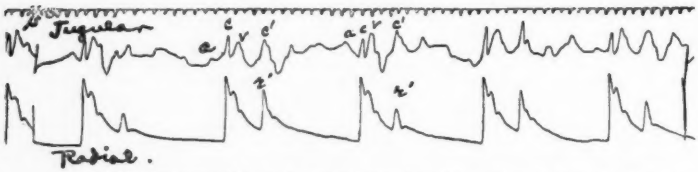

Fig. 79.—Polygraphic tracings of the jugular and radial pulse-waves showing pulsus bigeminus. The alternate smaller waves, *r'* and *c'*, are premature ventricular contractions.

overstimulated, with many futile and unavailing contractions. The waste of the heart's energy is at a maximum and exhaustion of its musculature follows (Fig. 80).

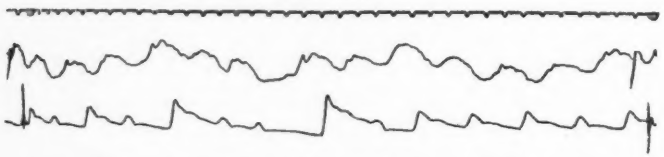

Fig. 80.—Absolute irregularity of the pulse due to fibrillation of the auricle.

Variations in the Rate of the Heart-beat.—Tachycardia, as before explained, may impair the circulation. The beats, following each other in rapid succession, do not permit of proper

filling of the ventricle. To maintain the circulation a slower rate would suffice. The heart, acting rapidly, is therefore working out of proportion to the demand put upon it, and easily becomes fatigued. During tachycardia the heart is smaller in its diastolic phase than in normal diastole. With fatigue of the left heart dilatation takes place, systolic contractions become

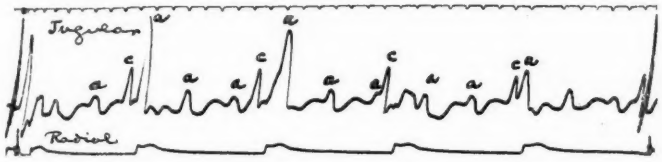

Fig. 81.—Tracings showing complete heart-block. The rhythm of the auricle differs and is entirely independent of that of the ventricle: a = systole of the auricle; c = systole of the ventricle.

incomplete, and each diastole finds the heart wider than before. In this way a state of tachycardia, apparently harmless, without any organic basis, may become clinically extremely significant. Disturbances of conduction resulting in prolonged diastole cause an increased intraventricular tension (Fig. 81).

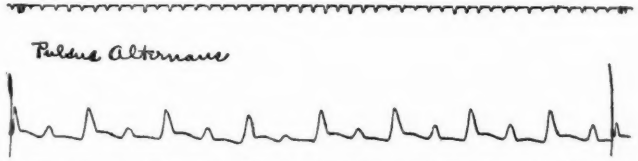

Fig. 82.—Pulsus alternans. Every alternate wave is small, each pulse period is of equal duration.

Pulsus Alternans.—Alternation of the heart indicates a state of myocardial exhaustion. The real cause of this form of the pulse-wave is not absolutely defined. "The disturbance is dependent upon some unexplained anomaly of the ventricular systoles, whereby at each alternate systole of the left ventricle a greater or lesser quantity of blood is thrown into the systemic arteries." It occurs in cases of tachycardia where it does not seem to have any very serious import. It also occurs when the

heart-rate lies within normal limits, and at such times it is a sign of much clinical value. In the vast majority of cases it is associated with degenerative changes in the heart muscle. The alternation itself causes no symptoms except those referable to the myocarditis responsible for the pulse anomaly (Fig. 82).

Symptoms in Other Organs.—When the heart is forced to exercise for a period at the full extent of its power heart failure sets in. This produces an insufficiency of circulation in the various organs. The functional impairment of the latter may produce symptoms indicating the debilitated power of the heart.

The symptoms of heart failure, therefore, are very variable, depending upon which organs in different individuals are most affected by the deficient blood-supply.

Stasis in the Pulmonary Capillaries.—Dyspnea is one of the earliest symptoms of functional disturbance of the heart. The respiratory center is extremely sensitive to changes of the O_2 and CO_2 content of the blood. On this account it has been maintained that dyspnea results from insufficient oxygenation of the medullary center. This, however, has been contradicted by Kraus, who showed that the amount of O_2 taken up by the blood and of CO_2 given off per minute is practically unchanged in cardiac failure. That is, the rapid breathing induces a greater amount of air to enter the lungs per minute without altering the amount of oxygen taken up by the blood.

It is therefore probable that stasis in the pulmonary capillaries stimulates the vagus endings in the same way as does CO_2. The elasticity of the lung is probably diminished and its volume is increased.

This explanation of the dyspnea in heart failure finds support in the clinical experience that severe dyspnea—panting—is an early sign of mitral lesions, while in aortic disease it is a sign of severe decompensation. Welch demonstrated that in conditions in which the force of the left heart was impaired without impairment of the right, dyspnea and the other respiratory disturbances set in. Failure of the right ventricle substitutes a state of broken systemic compensation, and the dyspnea may become much relieved.

Associated with dyspnea, perhaps the earliest sign of heart failure will be found in the appearance of fine crepitations at the bases of the lungs. In patients with mitral lesions particularly the bases of the lungs will be found to show signs of edema at the early stages of break-down.

Edema and Other Stasis Phenomena.—Stasis phenomena in heart disease, such as edema, ascites, hydrothorax, are evidence of failure of compensation of the right side of the heart. When the force of the heart no longer maintains the arterial pressure at the height necessary for efficient circulation in the tissues, we get the symptoms in the remote organs, with the development of dropsy, ascites, and enlarged liver. The disappearance of dropsy is often a definite sign of the restoration of the heart's tone.

Auscultatory Signs of the Functional State of the Heart.—Auscultation will yield much valuable information as to the sufficiency of the heart. If there is an insufficiency of the power of the left ventricle through diminution of its contractility or elasticity, the aortic second sound will show a relative reduction in intensity following brief exercise, owing to a smaller systolic output of blood. If, under such circumstances, the right ventricle remains sufficient, there will be a simultaneous accentuation of the second pulmonic sound. Cases which present this combination of signs are likely to end favorably.

Insufficiency of the right ventricle also is shown by a relative diminution in the intensity of the pulmonic second sound following exercise, and when this is combined with evidence of sufficient power of the left ventricle the prognosis is less favorable.

TESTS DEPENDING UPON CHANGES OF PULSE-RATE

1. Effect of changed position upon the pulse-rate.
2. Effect of exercise upon the pulse-rate.

The Effect of Changed Position upon Pulse-rate.—As early as 1833 Donnell showed that the pulse-rate is normally slower in the recumbent than in the erect or semi-erect positions. Schapiro made the observation that the normal difference disappears when the heart is seriously weakened. In 100 cases recently tested by Cabot and Bruce it was found that the slowing of 7

to 15 beats per minute, which recumbency normally produces, is diminished or altogether lost in cases of incompetent valvular disease, or when the heart is seriously weakened by any cause. Geigel found that a variation of pulse-rate above 30 between lying and standing indicates weakened heart function.

Psychic factors may considerably disturb the correctness of the estimate in any particular case. The normal increase from a reclining to a standing posture should never be more than 20 beats per minute.

In a group of 124 normal cases studied by Kahn the pulse-rate rose an average of 25 beats from the standing posture, as

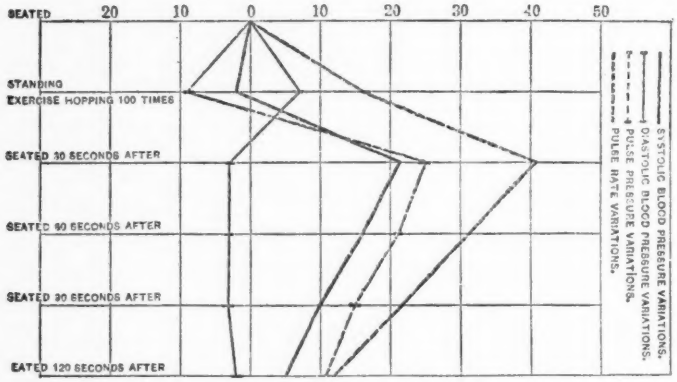

Fig. 83.

counted immediately after exercise, or of 41 beats from the seated position. Hopping 100 times on one foot was the exercise used. During the two minutes following the exercise it fell an average of 29 beats with the patient seated. There were no extreme variations in these figures, so that the results here obtained, and as shown in Fig. 83, may be taken as the normal pulse variations from the seated to the standing postures, and also following the prescribed form and degree of exercise.

Effect of Exercise on the Pulse-rate.—The variations of the pulse-rate following exercise were the first functional tests to be studied. Mendelsohn and Graüpner suggested the time it takes

for any given heart to return to normal after a definite amount of exercise as a measure of its functional capacity. The longer the time it takes to return to the normal rate, the less efficient they considered the heart.

The technic of the test is very simple. The pulse-rate is noted after a period of rest in the standing and the recumbent postures. The patient then performs a measured amount of work either on a Graüpner ergostat or in any other way. Cabot and Bruce use stair-climbing, and calculate the number of foot-pounds of work by multiplying the height climbed by the weight of the individual in pounds. The pulse is counted at rest after the work stops, and the time noted until its return to normal.

Mendelsohn asserts it as a principle that the greater the amount of work done with prompt return to the normal rate, the greater is the functional capacity of the heart. He emphasizes the point that the amount of work should be considered as of relative value only. Absolute amounts of work cannot be laid down as the normal for any person, because the capacity for work varies with the weight, muscular development, and general make-up of the individual.

METHODS DEPENDING UPON BLOOD-PRESSURE ESTIMATIONS

1. Tiegerstedt's factor.
2. Cardiac strength—cardiac weakness factor.
3. Phase variations of Tornai.
4. Effect of change of posture on the blood-pressure.
5. Effect of exercise on the blood-pressure.
6. Effect of compression of femorals.
7. Delayed rise of blood-pressure following exercise.

INSTRUMENTAL STUDIES OF HEART FUNCTION

Methods of Measuring the Blood-pressure.—Digital examination of the pulse reveals a number of important data. The palpation of the arterial wall, the resistance it offers to the compressing finger, the size of each beat, the manner of its rise, the duration of the pulse-wave, and the diastolic pressure after the wave has subsided—are indicators of value, some of which the

finger alone can detect. This method, however, offers no mathematical accuracy in interpretation, and must, therefore, be supplemented by the instrumental methods which have come to play a most important rôle in the study of the circulation.

The instruments used are in the main mechanical variations of the Riva-Rocci type. They all consist of an inflatable air-bag which surrounds the arm. Hill and Barnard's instrument consists of a small bag which is applied over the radial artery. The bag is connected by a tube to a mercury, com-

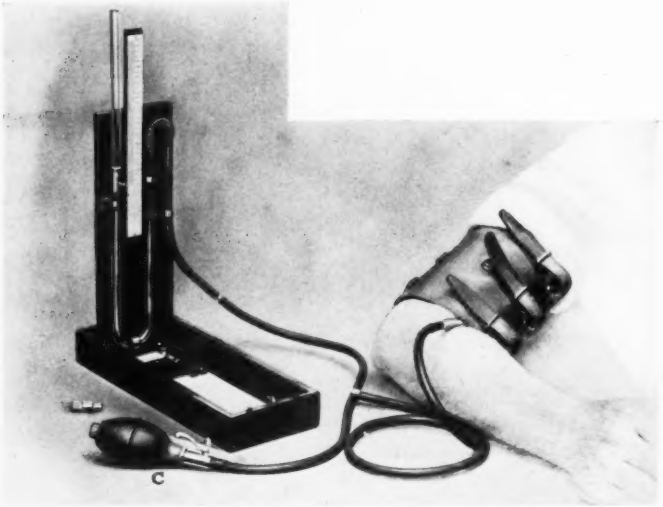

Fig. 84.—Dressler's modification of Janeway's sphygmomanometer.

pressed air, or spring manometer. The bag is inflated through another tube and the pressure read off directly from a scale on the manometer (Fig. 84).

The deduction is that the amount of pressure required to just obliterate the pulse is exactly equivalent to the intra-arterial blood-pressure. One important source of error must not be overlooked. It was formerly assumed that a very small amount of pressure would suffice to completely compress the normal

artery. This was evidently fallacious, as it has been definitely shown that it may require a considerable amount of pressure, even up to 30 mm. of mercury, to overcome the resistance of the arterial wall alone in certain cases in which the artery is thick, contracted, or sclerosed.

Method of Auscultatory Blood-pressure.—Korotkow, in 1905, first advocated the use of the auscultatory method of estimating blood-pressure. The usual cuff and manometer are used. A stethoscope is applied 2 to 4 cm. below the cuff over the brachial artery. The blood current is shut off, and when the mercury is permitted to fall gradually a clear tone is heard corresponding to the point of maximum systolic pressure. A sequence of sounds then follows as the pressure is gradually reduced in the cuff, until all sound disappears from the brachial artery; sometimes a low, dull tone may persist. This point corresponds to the minimum or diastolic blood-pressure.

Numerous studies have been made to discover the significance of changes in maximal and minimal arterial pressures, and careful analyses of the cycle of sounds in the artery below the point of compression have suggested certain tests of myocardial function. The variable factors in blood-pressure estimations are the heart and the elasticity of the vessels.

Korotkow recognized three phases in the arterial tones produced by compression of an artery by a Riva-Rocci cuff: A maximum pressure tone; a minimum pressure tone, and a murmur mixed with these occurring at a variable point between the two. Later authors (Ettinger, Fischer) recognized a fourth dull tone below the highest diastolic point.

We need not enter into the theoretic considerations regarding the formation and interpretation of the sounds. The factors involved are: (1) The impulse given to the blood-current by the heart's contraction; (2) the suddenness of the distention of the vessel; (3) the amplitude of the blood-wave; (4) the diameter of the vessel, and (5) the resonating character of the cuff.

There are five phases described during the lowering of the external pressure from above the obliteration point:

1. A clear, sharp sound—the index of systolic pressure.
2. A murmur of variable duration replacing the above.
3. A clear, usually loud and snappy sound replacing the murmur.
4. A transformation (usually sudden, at other times more gradual) of the clear sound into a dull one, the index of diastolic pressure.
5. The disappearance of all sound.

The maximal blood-pressure in the arteries occurs during ventricular contraction. The diastolic is the minimal arterial pressure, and represents the ebb to which the arterial pressure falls while the aortic valves remain closed. V. Recklinghausen found that in taking the reading by the mercury manometer the large oscillatory waves which occur in the mercury column begin and end abruptly; and these points he considers the points of maximal and minimal pressure.

The amplitude or range of arterial pressure between systole and diastole is the result of the volume output into the circulation of the heart, and is called the pulse-pressure. It indicates the extent to which the heart overcomes the peripheral resistance. It represents that excess over diastolic pressure which opens the aortic valves and distends the arterial walls.

We shall concern ourselves with the significance of the blood-pressure as an index of the functional capacity of the heart.

The normal systolic blood-pressure of adults up to forty years varies from 115 to 125. It is less in younger individuals and females, and usually increases with age, so that a pressure of 140 to 150 may be considered normal in people over fifty years. The normal diastolic pressure ranges from 30 to 50 mm. of mercury below the systolic pressure.

Gibson has suggested that certain arithmetic relations normally exist between the three divisions of the blood-pressure:

Diastolic : Systolic = 2 : 3, and

Pulse-pressure : Systolic pressure = 1 : 3.

Based upon the ratio to each other of these factors certain methods have been suggested for the estimation of the efficiency of the heart considered as a pump.

Cardiac Efficiency Factor of Tigerstedt.—Tigerstedt utilizes the formula of Poiseuille, which is used for fluids circulating in horizontal tubes. Reasoning from that formula, he suggested the following:

The pulse-pressure or volume output of the heart multiplied by the pulse-rate represents the velocity of the circulation. The systolic pressure multiplied by the pulse-rate represents the total amount of work done in the circulation. The quotient of the velocity of circulation divided by the total work in the circulation gives the efficiency of the heart as a pump. Thus:

$$\text{Pulse-pressure} \times \text{pulse-rate} = \text{velocity.}$$
$$\text{Systolic pressure} \times \text{pulse-rate} = \text{work.}$$
$$\frac{\text{Pulse-pressure}}{\text{Systolic pressure}} = \text{efficiency of heart as a pump.}$$

This is called the blood-pressure coefficient. In the normal individual this coefficient is 25 to 35 per cent. A cardiac efficiency factor below 20 per cent. or over 40 per cent. would indicate myocardial inefficiency. To illustrate: A systolic pressure of 130 mm., while within normal limits, may, in truth, represent the total power of a failing heart if accompanied by a diastolic pressure of 110 and a pulse-pressure of 20 mm., as the formula would show:

$$\frac{\text{Pulse-pressure}}{\text{Systolic pressure}} = \frac{20}{130} = 15 \text{ per cent.}$$

The same conditions may be present with a high systolic and a high diastolic pressure. Great increase of the pulse-pressure is pathologic, and may be more than the normal heart can stand. The myocardium may, to a limited extent, hypertrophy to be enabled to bear the overload of volume output. If the overload becomes excessive and the heart begins to fail, the pulse-pressure would fall at the expense of the maximal pressure. Thus, in compensated and advanced arteriosclerosis and chronic interstitial nephritis, a systolic pressure of 180 to 200 mm., accompanied by a diastolic pressure of 110 to 120 mm., is frequently seen; and in such cases when the heart begins to fail the systolic pressure

falls, while the diastolic pressure, owing to the rigid arteries and the increased pulse-rate occasioned by the dilating heart, may remain relatively high. As a result the pulse-pressure falls until the head of pressure in the arteries is no longer sufficient to maintain the circulation.

Stone has suggested the determination of a cardiac load and overload factor, based on auscultatory blood-pressure determinations. He considers that the pulse-pressure measures the energy of the heart in systole in excess of the diastolic pressure. For clinical purposes it represents the load of the heart. Under normal conditions it is approximately 50 per cent. of the diastolic pressure. The myocardial load, according to Stone, may, therefore, be expressed by the fraction:

$$\frac{\text{Pulse-pressure}}{\text{Diastolic pressure}} \text{ or } \frac{\text{P.-P.}}{\text{D. P.}}$$

Since the diastolic pressure measures the peripheral resistance, it is a better index of hypertension than the systolic pressure. A sustained diastolic pressure of 100 to 110 signifies hypertension. The diastolic is less influenced by physiologic factors than the systolic pressure.

Cardiac Strength—Cardiac Weakness Factor.—By studying the relation of the five phases heard in auscultating the brachial artery, certain proportions of each to the pulse-pressure are maintained under normal conditions. These proportions have a functional significance. With decompensation or circulatory disturbances of lesser degree, the element of heart weakness (the first phase plus the fourth phase) progressively encroaches on the element of heart strength (the second phase plus the third phase). As a case of decompensation improves, the element of heart weakness gives place to the element of heart strength.

In cases of organic disease, where the function is impaired, as in myocarditis, the sequence readings may show no phases, or one phase may be lacking, usually the second or third; whereas in the neuroses no variations from the normal function will occur.

Goodman and Howell found the following percentages normal:

First phase	31.1
Second phase	44.4 to 55.5
Third phase	11.1
Fourth phase	13.3

The cardiac strength, as indicated by the sum of the second and third phases, bears normally a ratio of 5 to 4 to the sum of the first and fourth phases.

Phase Variations of Tornai.—Tornai discerns as many as six phases, and he bases the functional diagnosis upon certain variations in the relationship between these tones toward each other. It is important to eliminate as much as possible any excitement or undue strain.

In healthy people there is normally a period in the blood-pressure reading during which an arterial murmur is audible. This murmur increases in duration after moderate exercise and approaches the maximal point. Within three to five minutes after work, however, the normal heart returns to its normal phase relations. After fatiguing work eight to ten minutes may elapse before a return to normal. During this period, after engaging in fatiguing exercise, the maximal and minimal pressure, as well as the position of the murmur, are lower than before.

When we find, therefore, that after exercise the arterial murmur begins higher and nearer the maximal pressure, and that the maximal and minimal pressures have not fallen, we may conclude that the heart in that case possesses a sufficient reserve force (for the amount of work executed).

In heart disease diminished reserve force will be indicated by a shortening of the murmur phase and its depression after exertion.

In cases of marked hypertrophy of the left ventricle Tornai has found that a normal reaction to exercise may take place because of the increased output with each beat, although the functional capacity of the heart may be affected by its valvular trouble.

Normal Effect of Change of Posture upon the Blood-pressure.—The auscultatory method for blood-pressure examination should properly be applied with the patient's arm at the side of the chest, as the normal reading varies considerably with the arm in different positions.

This holds for both the seated and the standing postures and even in the recumbent position, and was carefully adhered to in all our observations.

Change of posture causes a vasomotor effect that manifests itself by change of systolic and diastolic pressure and of pulse-pressure. This is the more marked the greater and the quicker the change of posture is executed.

Crampton found that the systolic pressure is increased normally on change from the recumbent to the standing position, while in conditions of lowered vasomotor tone it remains the same or is decreased.

From the seated to the standing position the change is distinct and normally quite characteristic. In my group of 124 normal cases the systolic pressure fell an average of 2 mm. of mercury on assuming the standing position. In the large majority of cases the change ranged between a rise of 10 mm. or less and a fall of 10 mm. or less. In one case a rise of 26 mm. of mercury and in two cases a fall of 24 mm. of mercury were the extremes.

The diastolic pressure rose an average of 7 mm. from the seated to the standing posture. It rose in almost every case, and in a few cases as high as 20 mm. of mercury; in a few cases it fell 10 mm.; in only one case did it fall 27 mm. The pulse-pressure fell an average of 9 mm. of mercury on change from the seated to the standing position (see Fig. 83).

EFFECT OF EXERCISE ON THE BLOOD-PRESSURE

Stair-climbing Test of Selig.—Selig experimented with 100 persons in various states of health before and after exercise. The exercise consisted in stair climbing and, in several cases, a game of football. Immediately after the exercise the blood-pressure was taken.

In the normal cases the blood-pressure rose an average of 8 beats. In most of 46 cases of various general diseases the blood-pressure fell after the work. The results showed, however, a considerable difference between the various types of cases.

In the 43 cases which showed heart disease the blood-pressure rose an average of 10 mm. Hg. per minute. However, in some of these cases with valvular defects the climbing of as high as 2000 steps often did not fatigue; whereas in the cases of myocardial weakness even a very few steps were at times fatiguing, and these cases showed a dilated heart after any kind of light work.

This staircase test is perhaps the most commonly employed on account of its simplicity, and the fact that it can be performed without any special apparatus. We find almost always complete corroboration of the patient's statements regarding his cardiac capacity in doing this test. Stair climbing or merely walking is an experiment every cardiac patient necessarily performs upon himself in the usual course of his life, and the symptoms of fatigue come perhaps concomitantly with the physical signs we discover.

The "hopping test," or bending the knees or the trunk, are modifications of the Selig test. These are used not only for the study of heart function, but frequently as a routine method to elicit a latent valvular lesion.

Katzenstein's Test.—Marey and Weber found that the blood-pressure increases after ligation of a large artery, such as the femoral or iliac; or after compression of the abdominal aorta in laboratory experiments. If we increase peripheral resistance by suddenly diminishing the vascular field, a marked rise in blood-pressure occurs. The heart normally does not increase in rate, but there occurs an increase in the ventricular output, the strain falling directly upon the left ventricle, corresponding to the second form of heart reaction as before described.

Experimentally, hypertrophy of the ventricle takes place. In weak animals, however, the heart does not stand the increased strain, and dilates, the animal dying of heart failure.

This principle is used by Katzenstein as a test of the heart function. The patient lies quietly in the recumbent position. The pulse-rate and blood-pressure are carefully taken. Both iliac arteries are then compressed digitally by an assistant for two to two and a half minutes, although Katzenstein advises compression even up to five minutes. Compression may be made by an Esmarch bandage, or, according to Merelli, by an inflatable rubber cuff.

Katzenstein deducts the following standards from his clinical studies and animal experimentation:

1. In normal compensated hearts, after compression of the iliac arteries, the blood-pressure rises 5 to 15 mm. of mercury and the pulse-rate falls.

2. In hypertrophied compensating hearts the blood-pressure rises 15 to 40 mm. Hg. and the pulse-rate falls or may remain unchanged.

3. In beginning decompensation the blood-pressure remains unchanged while the pulse-rate increases.

4. In cases of cardiac decompensation the blood-pressure falls, while the pulse-rate increases considerably.

Pain is sometimes produced by the digital pressure required to obliterate the femoral or iliac pulse. The psychic influences here are particularly disturbing and the pain may of itself cause variations of pulse-rate and blood-pressure.

It is of interest that Katzenstein used the test to determine the risk and prognosis of anesthesia and surgical procedures on his cases. He found that an abnormal reaction to the test should interdict general anesthesia or major operations.

Barringer's Test of Functional Capacity.—Arno Lehndorff showed experimentally in 1908 that stimulation of the splanchnics produces their contraction with increase of blood-pressure to a varying degree. If the heart's action becomes insufficient, however, the blood-pressure falls. With the recovery of the heart's contraction the pressure rises again.

Recently Barringer described a test of heart function, using Graüpner's method of making frequent readings of the pulse-rate and systolic blood-pressure after measured amounts of work,

and clinically obtaining Lehndorff's experimental results in insufficiency of the heart.

The theoretic basis upon which he explains his test is as follows:

Muscular work increases the CO_2 content of the blood. This stimulates the nervous centers controlling the suprarenal glands. An increase in the adrenal content of the blood is thereby produced, which causes a constriction of the vessels in the splanchnic area and a resulting rise in blood-pressure. The quickened heart-rate accompanying muscular work causes an increase in the quantity of blood discharged by the heart per minute, and this also contributes to the rise in blood-pressure.

The systolic pressure during work, therefore, mounts rapidly, and the left ventricle finds it more and more difficult to expel its contents against this increasing resistance. At a certain height of aortic pressure the ventricle probably does not empty itself completely, and a steadily increasing volume of blood remains in the heart after each systole. In other words, an insufficiency exists. At this moment the Roentgen ray would possibly show a heart decidedly increased in size. If the work stops, the CO_2 content of the blood falls, the activity of the suprarenal gland decreases, and the splanchnic vessels relax. The blood-pressure, therefore, begins to fall. But the heart now works more efficiently against the lowered aortic pressure and expels a larger quantity of the increased residual blood at each stroke, until it finally empties itself completely with each systole. The increased quantity of blood which the recovering heart thus throws into the aorta more than compensates for the lowered pressure. The pressure, therefore, again rises briefly, and this delayed rise of blood-pressure after the cessation of muscular work is the significant point in Barringer's test.

When the work stops, if the heart is much dilated, it probably requires a short time to reach its maximum efficiency to expel its increased contents, and there results a slowly mounting blood-pressure.

Technic.—Graduated work is furnished by movements of flexion, extension, and swinging with iron dumb-bells weighing

from 3 to 20 pounds each. These afford a practical means of furnishing graduated work for testing the heart functioning capacity. Computation of the amount of work performed through dumb-bell exercises is made according to the following example: If a 5-pound dumb-bell is extended upward from the shoulder through 2 feet of arm length, 10 foot-pounds of work are performed with each extension. With a 10-pound dumb-bell 20 foot-pounds, or twice as much work, would be performed in the same space of time.

If the systolic blood-pressure reaches its greatest height not immediately after work, but from 30 to 120 seconds later, or if the pressure immediately after work is lower than the original level, that work, whatever its amount, has overtaxed the heart's functional capacity, and may be taken as an accurate measure of the heart's efficiency.

This, like other tests based upon blood-pressure findings, omits a very important factor which in life has an effect upon the cardiac efficiency. That is the psychic and nervous influences which are accountable for a great deal of what we call heart strain. In actual life the situations are not so simple as the lifting of a dumb-bell under a physician's direction. The complex processes of life call for cardiac reaction to visual and auditory stimuli and other sensations not measurable in terms of physical work. For example, while crossing a road the sudden approach of a vehicle will startle the patient. One cannot estimate in foot-pounds of work the effect the excitement has upon the heart; and until we can translate the indefinite effects into numerical data the problem of the heart's functional capacity with the exactions of ordinary living will be only incompletely solved.

Barringer found that the delayed rise in systolic blood-pressure was obtained after large amounts of work which varied normally according to the subject's physique and condition of muscular training.

I have used this test extensively, and find it a valuable method for ascertaining the capacity of the individual for muscular work. I have shown elsewhere that thyrotoxic cases and

cases of hypertension have a diminished capacity according to this test.

POLYGRAPHIC TRACINGS AND THEIR VALUE IN FUNCTIONAL DIAGNOSIS

The necessity for obtaining graphic records of the movements of the circulation is now universally recognized, but there has

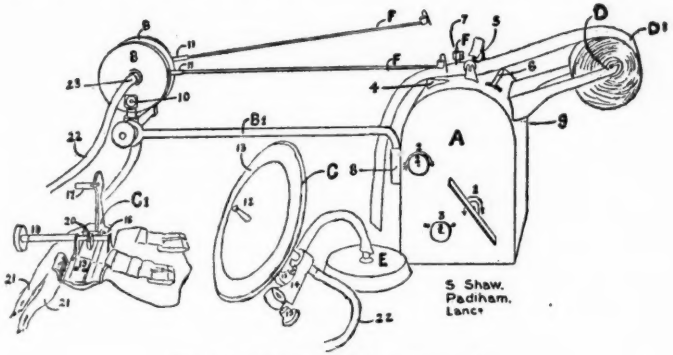

Fig. 85.—Mackenzie's ink polygraph.

hitherto been difficulty in obtaining a suitable instrument. Apart from the trouble of blackening and varnishing tracings, some methods are not convenient, especially when long tracings

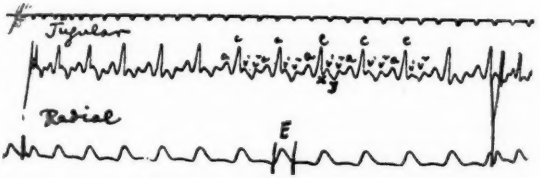

Fig. 86.—Tracings of the normal pulsation in the jugular vein: *a* is the auricular wave; *c*, the carotid wave; *v*, the ventricular wave; *E*, the sphygmic period.

are required. The ink polygraph meets the necessary requirements, as it enables tracings to be taken of any length, and after a little experience it is very easy to use. In investigating any

movement caused by the circulation it is necessary to record at the same time some standard event whose position in the cardiac cycle is fixed and determined. Hence it is necessary that two events should be simultaneously recorded—the one to be investigated and the standard movement. The best and most reliable standard movement is the arterial pulse, radial and caro-

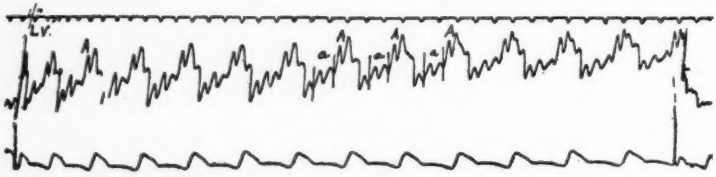

Fig. 87.—Cardiogram from a case of mitral stenosis, presenting graphically the presystolic thrill at the apex of the heart.

tid. With the ink polygraph these movements can be recorded by one lever, while the movement to be investigated is recorded by the other lever. Other movements, as those of the respiration, can also be recorded (Figs. 85–89).

The radial sphygmograph is of value as an indication of the occurrence of ventricular systoles, and for calculating the

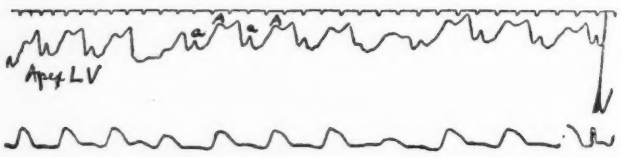

Fig. 88.—The apex-beat and radial pulse in a case of marked myocardial degeneration. Note the prominence of the *a* wave due to loss of tonicity of the ventricular wall, permitting the auricular impulse to directly affect the chest wall. The radial wave shows pulsus alternans.

sphygmic period. A small amplitude in the radial tracing will, therefore, be sufficient. The venous pulse is more easily obtained on the right side with the head turned to the left and the chin elevated. To fail in obtaining a record of the venous pulse is the exception rather than the rule; but it is practically impossible

in some cases, especially in an emphysematous chest with dyspnea.

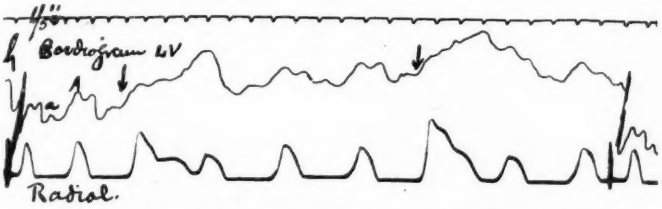

Fig. 89.—The effect of cough in marked myocardial degeneration. Mere coughing causes sudden increase in ventricular dilatation with a resulting increased systolic output, giving the peculiar tracing here recorded. This is pathognomonic evidence of very marked myocardial deficiency, as shown by the author elsewhere.

THE ELECTROCARDIOGRAM AND ITS VALUE IN FUNCTIONAL DIAGNOSIS

Every muscular action in the body is accompanied by the generation and conduction of an electric current. The human body may therefore be regarded as a battery, with the two arms and the two legs as its natural and convenient poles. When the body is at rest the predominating electric current is that associated with the contraction of the heart muscle.

If now, with the body at rest, the two hands or one hand and one foot are connected by wires into a circuit, with a very sensitive galvanometer between them, each time that the heart beats the needle of the galvanometer will be deflected to one side or the other, depending upon the direction of the current; and the extent of its deflection will be proportionate to the amount of current and the difference in potential between the two poles. Not only will the galvanometer needle be deflected each time that the heart beats, but it will be deflected with the auricular contraction first and then with the ventricular contraction separately. A graphic record of the deflections can be obtained by photographing the movements of the needle on a moving film.

Einthoven, of Leyden, invented a galvanometer which is exceedingly sensitive to very minute electric currents or differences

in potential. It consists of a fine quartz or platinum thread suspended vertically in an electromagnetic field. Its ends are

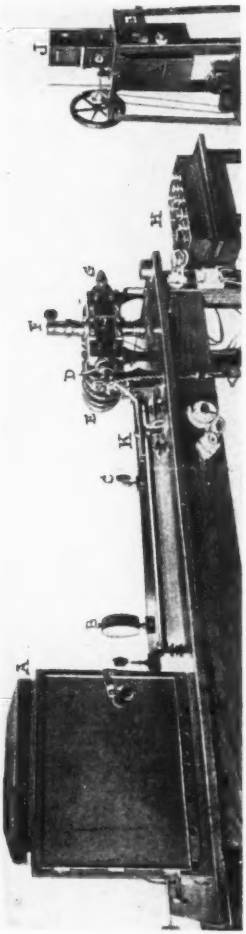

Fig. 90.—The Williams-Hindle electrocardiograph: *A* is the lamp-hood which encloses the Cunningham arc light; the rays then pass through the condensing chamber at *B*. *C* is the target by which the beam of light is directed on the anterior microscope *D*. *E* is the electromagnet, in the center of which is the string-housing *F*, which protects the delicate string which is actuated by heart-currents. *G* is another microscope for further magnification of the string shadow. *H* is the resistance box which controls the current passing through the string and which protects against induction currents. *J* is the camera, camera motor, and 200-feet film roll. *K* is the tuning-fork which marks the abscissæ on the electrocardiogram.

connected by wires to the poles of the body to be examined. When the current from the body passes through the thread it is

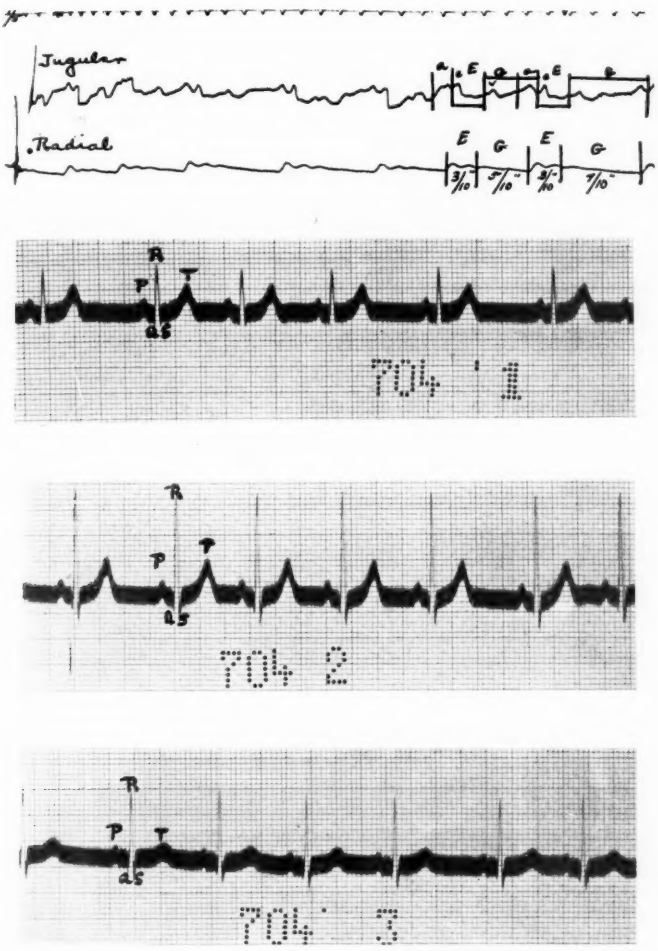

Fig. 91.—Youthful type of irregularity, showing the regular duration of the systolic period *E* and marked variation in the diastolic period *G*. The jugular tracings show that the right auricle (*a*) and ventricle (*c*) participate in the same irregularity as the radial pulse. The presence of this type of irregularity is not significant, and, according to Mackenzie, indicates that the heart is healthy. The electrocardiographic records are from the same case and are normal.

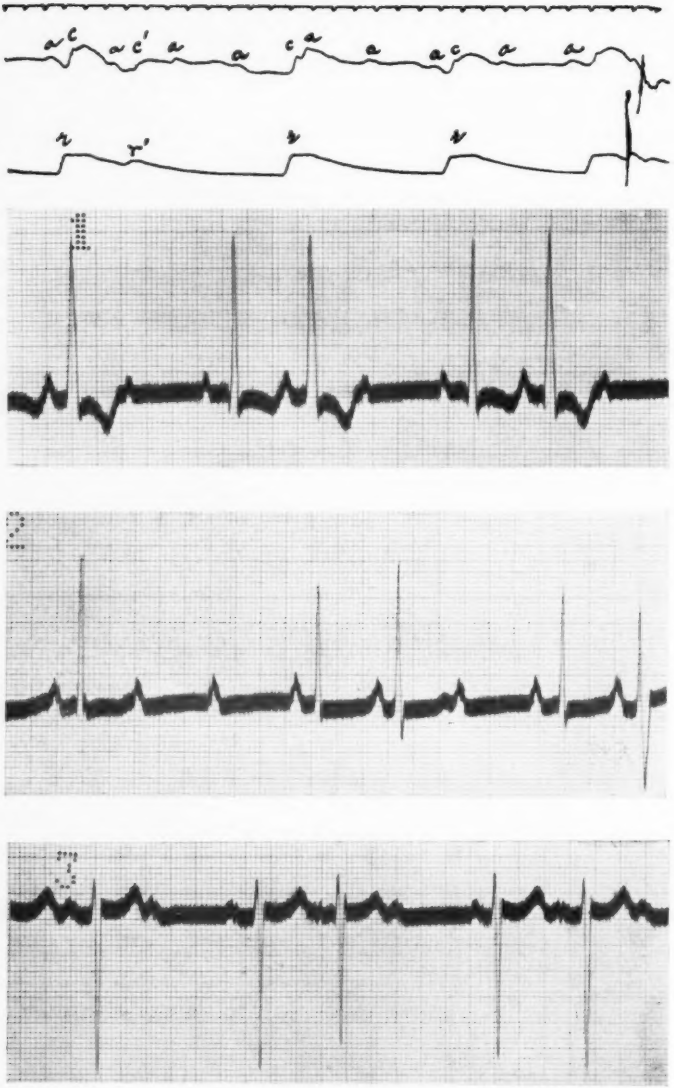

Fig. 92.—Polygraphic and electrocardiographic records from a case of partial heart-block, showing periods of 1 : 1, 2 : 1, and 3 : 1 rhythm. The 3 : 1 rhythm allows the conductivity of the *a-v* bundle to recover, and this results in a 1 : 1 period.

attracted to one or the other side of the magnetic field. This thread is magnified by a powerful lens and is illumined by a powerful arc-lamp. Its shadow is focussed on a camera in which it is photographed on a moving film (Figs. 90–95).

By this method it is possible to study very small currents. The electric variations accompanying the cardiac action have an intensity of from 1 to 3 millivolts. The current is led off through the string in three directions: *Lead I* contains the right hand and the left hand in the circuit; *Lead II*, the right hand and left foot; and *Lead III* carries the current from the left hand and left leg. The current from the body enters the string at its upper end. An electrocardiogram is obtained from each of the three leads in cases studied. The normal electrocardio-

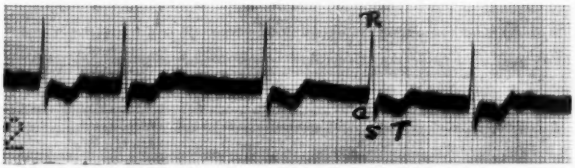

Fig. 93.—Electrocardiogram in a case of auricular fibrillation. Note the absence of the *P* wave. Inversion of the *T* wave is evidence of the effect of digitalis on the heart.

gram consists of a series of waves, the result of auricular and ventricular activity (Fig. 91).

As can be seen, the first wave is small and is due to the activity of the auricle—designated by Einthoven the P wave. This is followed by a very small depression of the curve below the base line, and is called the Q depression. Then come a series of waves due to the action of the ventricles: a large wave R, which rises suddenly and falls to below the base line (the S depression), and finally a second smaller wave, T, which occurs during the middle of systole.

Observations made by Lewis and Gilder indicate that certain clinical valvular conditions cause more or less typical changes in the form of the waves of the electrocardiogram.

In mitral stenosis the average curve in Lead I shows a diminution of R, and increase of S; in Lead III it shows a conspicuous increase of R and a decrease of S, as compared to the normal. This is the sign of right ventricular preponderance, as shown by Einthoven. The right side may be so predominatingly hyper-

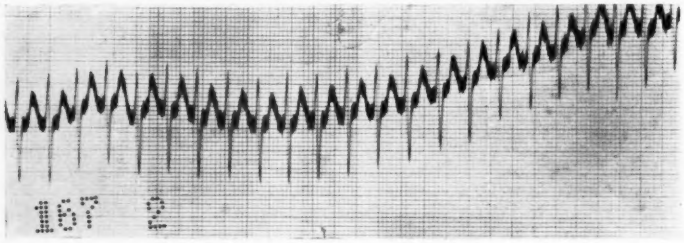

Fig. 94.—Electrocardiogram from a case of paroxysmal tachycardia with a rate of 214 beats a minute.

trophied as to cause an actual inversion of R, below the base line in Lead I.

In aortic cases, on the contrary, the picture is reversed. In Lead I, R is increased and S diminished; while in Lead III, R is diminished and S is increased. In more marked hypertrophy R in Lead III is inverted below the base line. These changes constitute the right or left ventricular preponderance.

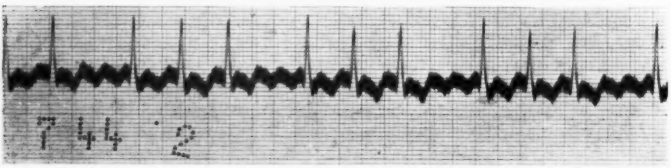

Fig. 95.—Electrocardiogram taken during an attack of auricular flutter.

Defects of conduction are clearly shown by the electrocardiogram, and a reference to the accompanying figures will show the electrocardiographic evidence obtained in a wide variety of cases.

Electrocardiographic Changes Associated with Myocardial Involvement with Special Reference to Prognosis.—What is

probably the most important advance in the interpretation of the electrocardiogram, with particular reference to the estimation of myocardial involvement and prognosis, has recently been made by Oppenheimer and Rothschild, and reported by them from the Electrocardiographic Laboratory of Mount Sinai Hospital. I shall quote freely from their publications on the subject:

"The normal electrocardiogram is to be considered the result of the passage of an impulse at a normal velocity through the usual channels; that is, node of Tawara, main stem, bundle

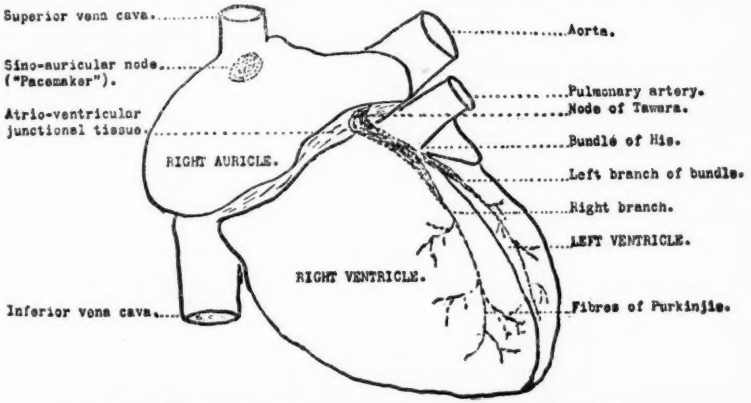

Fig. 96.—The conduction system of the heart showing in shadow diagram the approximate relation of the more recently discovered structures to familiar anatomic divisions of the heart (after Smith).

branches, and arborizations, which consist of the so-called Purkinje fibers. The latter form a network covering practically the entire endocardial surface of the ventricles. The velocity of the impulse through Purkinje fibers is at least ten times faster than its rate through ordinary ventricular musculature. The impulse reaches the ventricle normally through the Purkinje fibers, stimulating the ventricular walls practically as a whole.

"It is conceivable that the passage of this impulse may be hindered at any point in the conducting system.

"A lesion only partly involving either bundle branch, or an

extensive lesion of the arborizations of a branch such as occurs in human pathology, would cause a delay in the transmission of the excitation wave to the area supplied by the damaged conduction fibers. Such a lesion if sufficiently extensive should give observable changes in the electrocardiogram, and it is probable that these changes will be distinguishable from the changes that are produced by most other cardiac abnormalities.

"By intraventricular block is meant any delay in conduction below the main stem of the bundle of His. Intraventricular block includes: (1) Bundle branch block, and (2) arborization or Purkinje block, by which we mean interference with the conduction beyond the two chief branches of the bundle of His.

"This disturbance of conduction may be permanent or temporary. The permanent changes are indicative of a definite pathologic lesion, generally myodegeneration.

"The criteria in this form of electrocardiogram are, in general, as follows:

"1. Abnormal prolongation of the time interval of the QRS group beyond the normal limit of 0.1 second. This prolongation is most manifest in a widening of the R wave, so that its foot-points are abnormally separated. The R wave no longer has its slender, tall, spine-like appearance, but is broader and sometimes blunter than normally.

"2. Notching of the R wave. This notching may appear on the ascending or descending limb, on both limbs, or at the peak. It may be multiple, and its degree and location may vary slightly from beat to beat. In arhythmias the shorter the preceding intraventricular interval, the more pronounced is the evidence of disturbed intraventricular conduction.

"3. Low voltage as expressed by a low amplitude of the waves in all three leads. This change is not uniformly present, but when it occurs it helps to differentiate this type from the electrocardiograms typical of bundle branch block.

"4. Absence of the typical diphasic curves with huge T waves found in experimental bundle branch block.

"*Prognosis.*—Special emphasis should be laid on the serious prognosis in patients showing electrocardiograms indicative of

intraventricular block. Of the patients whose fate is known, the mortality has been 48 per cent. within two years.

"On physical examination two signs have been especially noted: (1) A muffled, poor, or practically absent first heart sound, and (2) a gallop rhythm. One is often struck by the fact that the heart is hypertrophied, but that the first sound, instead of being booming, has a poor or muffled quality."

VITAL CAPACITY OF THE LUNGS AS A TEST OF MYOCARDIAL FUNCTION

It has long been known that in patients with heart disease the vital capacity of the lungs, that is, the volume of the greatest possible expiration after the deepest inspiration, is decreased below normal. Determinations of the vital capacity in cases of cardiac disease are often of practical value, as they give quantitative information as to the tendency to dyspnea, and thus, indirectly, as to the clinical condition and the reserve power of the patient.

Peabody has made extensive graphic and clinical studies of the respiration by means of the following method:

Briefly, it consists in having the subject breathe through valves which separate the expired from the inspired air. The expired air passes through a closed circuit and is then rebreathed, so that the inspired air contains a progressively rising percentage of carbon dioxid and a falling percentage of oxygen. Samples of the inspired air are then taken every two minutes and analyzed for carbon dioxid. A calibrated volumetric recording spirometer is connected with the closed circuit, and the volume of each respiration is registered on the drum of a kymograph. With the aid of an electric timer the minute-volume of air breathed can be thus easily determined.

From the studies of Peabody and his collaborators it is evident that there exists a remarkably close relationship between the clinical condition of cardiac compensation and the vital capacity of the lungs. Thus, in general, patients with a vital capacity of 90 per cent. or more of the normal standard adopted for their sex and height have little or no abnormal tendency to

dyspnea. Patients with a vital capacity of from 70 to 90 per cent. of the normal become short of breath on unusual exertion and must lead a restricted life, although many of them can do light work. Patients with a vital capacity of from 40 to 70 per cent. of the normal are much more limited in their activities. They become dyspneic on moderate or slight exertion, are rarely able to work, and frequently suffer from cardiac decompensation. Those with a vital capacity of less than 40 per cent. of the normal are decompensated patients, usually confined to bed, and the mortality in this group is high. There is, moreover, a close correspondence in the individual case between changes in the vital capacity and variations in the tendency to dyspnea. In stages of decompensation the vital capacity falls; and with recovery, the vital capacity rises.

THE MYOCARDIAL RETRACTION REFLEX

Attention was directed to a heart-reflex in 1898 by means of *x*-rays, and it has since been suggested as of value in determining myocardial tonicity.

The reflex under consideration consists of a contraction of the myocardium of varying duration, which results when the skin of the precordial region is irritated. The cutaneous irritant may vary from a spray of ether to rubbing with a towel, or by a series of percussion blows. The most effective site for inducing the heart-reflex is the spinous process of the seventh cervical vertebra.

In very large dilations and in advanced myocardial degeneration the heart does not respond to precordial excitation.

MYOCARDIAL DILATATION REFLEX

A counter-reflex exists of dilatation of the heart muscle as a result of peripheral irritation. This may be evoked by percussing the spinous processes of the ninth, tenth, eleventh, and twelfth dorsal vertebræ. This reflex has not been studied with regard to its evidence in cases of myocardial insufficiency.

THE ELIMINATION OF SALT AS AN INDEX OF HEART FUNCTION

Korányi's method is based upon the principle that the concentration of the urinary ingredients depends upon the velocity of the circulation. Therefore, with reduced circulation, NaCl output will be reduced; and with acceleration, it will be increased. Therefore the molecular concentration of NaCl in the urine as measured by the freezing-point may be regarded as a test of circulatory efficiency; *i. e.*, $\frac{\Delta}{NaCl}$ is increased in slowing circulation and lessened by rapid circulation.

Korányi examined twenty-four-hour urinary collections. Loeb and Knecht modified the method as follows: The patient takes his evening meal at 6 P. M. He voids at 12 midnight and 6 A. M. He then gets 100 gm. milk, and after that urinates every one and a half hours. These urinary portions are each examined for $\frac{\Delta}{NaCl}$. These specimens of urine are not affected by previous ingesta. The effect of exercise can then be studied as has been done by Loeb, and more recently by v. Ritook.

The latter compared the Korányi test with the v. Recklinghausen-Strassburger test in the same cases. He examined 41 cardiac cases almost decompensating.

The urine of $1\frac{1}{2}$ hourly fractions was first examined, and at the same time the pulse-rate (F), the minimal B.-P. (D), and systolic pressure (S) were taken.

$S - D =$ amplitude (A), from which is derived $\frac{A}{S} = Q$ (Strassburger's Quotient), and $A \times F$ is calculated.

Then the patient was given some work on the ergostat, the pulse- and blood-pressure again taken, and after one hour the urine again studied for $\frac{\Delta}{NaCl}$.

The authors frequently found contradictory results. They found that the amplitude estimation as a test of beat volume and the $A \times$ pulse-rate as an index of rapidity of circulation are not accurate. This was also found by Klemperer.

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CLINIC OF DR. ALBERT R. LAMB

PRESBYTERIAN HOSPITAL

THE FLINT MURMUR

THIS afternoon I wish to present to you, briefly, two companion cases to emphasize some points in regard to the so-called "Flint murmur." It is with some hesitation that I place so much stress upon cardiac murmurs, as all our endeavor has been to induce you to think less about murmurs and more about the other factors which spell cardiac compensation or insufficiency. However, murmurs cannot be entirely neglected, and upon this particular murmur there is always more or less loose speculation and talk. Furthermore, it involves the definite decision as to whether the sound is purely functional or is indicative of a real mitral lesion causing stenosis. If anything can be brought out to help you in reaching a clear and logical conclusion in these cases, it seems to me worth while. I do not propose to go into each of these cases at great length, but merely to point out the salient facts which have to do with our present discussion.

CASE I.—H. W., female, age twenty-two, entered the hospital December 25, 1917, and died January 4, 1918. Previous to this she had been treated in the hospital and out-patient department for a period of six years. Her history is one of repeated attacks of acute rheumatic fever, starting at the age of eight, with symptoms of cardiac insufficiency from the age of eleven. While in the hospital in 1912 the examination of her heart is recorded as follows: Action forcible, with heaving of entire precordium. Apex in fifth space 12½ cm. to the left of the midline. Left limit of dulness in same space 14½ cm. to the left. Right border at the right sternal margin. At the apex there is a soft blowing

systolic murmur. At the base there is a systolic murmur, and a louder diastolic, which is transmitted downward across the sternum. There is a *presystolic rumble at the apex, probably a Flint.*

On her final admission the examination is very much the same except that the heart is considerably larger. The following note is made: "At the apex there is a rumble in presystole—Flint murmur(?)."

Her final clinical diagnosis was mitral and aortic insufficiency, indicating that her presystolic murmur was considered a Flint.

Autopsy.—The tricuspid and pulmonary valves are normal. The left ventricle is markedly dilated. The mitral valves are much thickened throughout, but especially along the borders. The adjacent edges of the cusps are firmly fused. The chordæ are thickened and shortened. The aortic cusps are similarly thickened throughout.

CASE II.—A female, colored, aged twenty-six, single, entered the hospital March 1, 1917, and died April 2, 1917. Her complaints were those of cardiac insufficiency. Careful questioning failed to elicit any history of acute rheumatic fever or any of its manifestations. She had a child at the age of fourteen. No history of venereal infection. Wassermann: alcoholic antigen negative, cholesterin antigen +++. Both antigens negative on repetition. Examination of heart was as follows:

Cm. to right.	Space.	Cm. to left.	
	ii	3	Apex impulse diffuse, with
2.5	iii	6	maximum in fifth space 13
3.0	iv	10	cm. to the left of the mid-
	v	15	line.
	vi	16	

At the apex the first sound is long and rough, probably preceded by a rumbling presystolic murmur. It is followed by a blowing systolic murmur heard all over the precordium. The second sound is not clear. Followed by diastolic murmur. At the base there are systolic and diastolic murmurs.

Note (March 3d).—The presystolic murmur at the apex is very short, does not end with a flapping first sound, but fuses

with the systolic murmur. Knee-jerks sluggish; Achilles' jerks only barely obtained.

Note (March 21st).—Heart outline somewhat larger. There is a rough presystolic thrill and a crescendo presystolic murmur beginning in early diastole. *This may be a Flint murmur.*

Clinically the case was considered syphilitic aortitis, and specific treatment was used.

Autopsy.—The valves of the right side of the heart are normal. The mitral ring is moderately dilated, the valves being quite normal in appearance. The aortic ring is unusually wide, the cusps are thickened. The edges are rolled and scarred. The aorta is unusually free from sclerosis in the arch and is quite elastic. Just above the aortic valves, however, there are one or two small reddish-gray raised plaques. These show microscopically a typical, active syphilitic process.

Discussion.—Thus we have two cases in each of which it is suggested that the presystolic murmur may be a Flint. As you have learned from the autopsy abstracts, this supposition was correct in one case and wrong in the other. The point of our discussion today is to determine whether there is any way to avoid these errors. Has any one any suggestion to make?

STUDENT: One might tell from the character of the pulse.

DR. LAMB: Yes, there are certain signs which we are accustomed to associate with the diagnosis of a Flint murmur. The most important of these are the presence of the Corrigan pulse, the absence of the tapping systolic impulse and snappy first sound of true mitral stenosis, and the form of the cardiac enlargement. The character of the murmur and the presence or absence of a thrill have very little value. I do not wish you to disregard these various points in differential diagnosis. You will find an excellent account of them in Thayer's articles published in 1901. Today, I do not wish to dwell upon them, but rather to look at the problem from a little different angle, for it is certain that mistakes in diagnosis are frequently being made in spite of attention to the above factors.

We are always on more secure ground when we get back to the etiology and pathology of any given condition, and I think

it will pay us to look at the problem of the Flint murmur from this viewpoint if we wish to make its diagnosis more certain. It is a murmur made at the mitral orifice without changes in the segments of that valve, when there is an aortic insufficiency present. We need not go into the actual mechanism of its production, about which there has been considerable discussion since Flint first called attention to the murmur in 1862. The point is that there must be an aortic insufficiency present and there must not be changes in the mitral valve sufficient to cause a presystolic murmur. In other words, we wish to know under what circumstances we may have an aortic insufficiency without stenotic changes in the mitral valve. For to diagnose a Flint murmur, even if every differential diagnostic point favors it, when your knowledge of etiology and pathology warns you that there are almost certainly changes in the mitral valve segments, is to barter away every vestige of logical deduction which you may have.

Now what is the disease, par excellence, which causes uncomplicated aortic insufficiency?

STUDENT: Rheumatic fever.

DR. LAMB: I think that you know better than that, and presume that you mean that rheumatic fever is the most frequent cause of endocarditis in general. That is quite correct. But it is not the most frequent cause of aortic damage *alone*. As a matter of fact, it is so rare for rheumatic fever to affect the aortic valve alone that for all practical purposes it may be disregarded. During the past three and a half years we have had autopsies on only 5 cases of chronic cardiac valvular disease due to rheumatic fever in which *the aortic valve was affected*, and in *every one of these there were very definite changes in the mitral valve as well.* Lees and Poynton in an analysis of autopsies on 150 cases found no case in which the aortic valve was affected without concomitant affection of the mitral valve. Now, as you know, we have all learned, I hope, that we cannot use the terms "never" and "always" in medicine. We should not say that we "never" have aortic insufficiency alone as a result of rheumatic fever, but that it is so exceedingly rare that it need not be seriously con-

sidered. Bearing the above facts in mind, it seems very easy to have avoided the error in the first case presented to you today. Here was a young woman who had had repeated attacks of rheumatic fever with symptoms of cardiac involvement for eleven years. Apart from any points of differential diagnosis, the possibility of a mitral presystolic murmur representing anything other than a mitral stenosis in her case is practically nil. I think that you will see that such a conclusion is logically reached in such a case. Therefore the first point which I wish you to carry away today is this: If there be a mitral presystolic murmur associated with an aortic insufficiency in a case giving a history of rheumatic fever or its manifestations, you will do well to ascribe such a murmur to an actual change in the mitral valve and not call it a Flint murmur. If you will remember this you will save yourselves chagrin at an unnecessarily wrong diagnosis on many an occasion.

We shall leave this aspect of the discussion to return to the question of the most frequent cause of uncomplicated aortic insufficiency.

STUDENT: Syphilis.

DR. LAMB: Yes, I think no one would venture to dispute this at the present time. Longcope's combined figures in 229 cases of aortic insufficiency give 74.2 per cent. of positive Wassermann reactions. This figure is conservative and indicates the exceedingly important rôle which syphilis plays in aortic insufficiency. It is also well recognized that the aortic insufficiency thus caused is almost always uncomplicated by stenotic changes in the mitral valve. Thus in 7 cases of syphilitic aortitis with aortic insufficiency which have come to autopsy at the Presbyterian Hospital in the past three and a half years, in none has there been changes in the mitral valve. In other words, we have the condition in which we should expect a Flint murmur. That this is not "always" the case is indicated by one of Longcope's cases, in which at autopsy there was an associated mitral stenosis. "Whether the mitral stenosis was a result of the syphilitic process, or caused by some acute infection, such as rheumatic fever, of which there was no history, could not be determined." In

this connection it is interesting to read over Flint's original articles. The case reports are brief, but there is more than a possibility that they were all three examples of syphilitic aortitis. Now, don't misunderstand me. I am not trying to argue that one finds the Flint murmur in cases of syphilitic aortitis only, nor that a mitral presystolic murmur occurring in that condition must be absolutely a Flint. The point which I am making is that Flint murmurs occur only in cases of aortic insufficiency uncomplicated by stenotic changes in the mitral valve, and that as syphilitic aortitis is the condition above all others which fulfils this requisite, you will do well to think long and hard before ascribing a mitral presystolic murmur occurring in a case of syphilitic aortitis to mitral stenosis. The second case presented to you bears this out.

One might bring up other etiologic factors and amplify the present discussion, but it has been my present intention to bring out these two most important points, *i. e.*, that without most convincing reasons you should not

1. Call a mitral presystolic murmur in a case of aortic insufficiency, due to rheumatic fever, a Flint murmur, or

2. Call a mitral presystolic murmur in a case of aortic insufficiency due to syphilis a murmur of mitral stenosis.

If you will remember these two points you will not only save yourselves from unnecessary mistakes in diagnosis, but you will train yourselves to look at the underlying causes of the conditions which confront you and approach closer to a proper unraveling of the more complex cases where the conditions mentioned coexist and where you are dealing with other etiologic factors.

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CLINIC OF DR. A. S. BLUMGARTEN

LENOX HILL HOSPITAL[1]

VAGOTONIA AND SYMPATHICOTONIA AS AIDS IN THE DIAGNOSIS AND TREATMENT OF ENDOCRINE CONDITIONS

Full Explanation and Meaning of Terms and Conditions; Illustrative Cases with Full Discussions of Treatment in Each Case.

WE shall discuss a number of endocrine conditions this afternoon, and shall lay particular stress upon the methods of diagnosing these lesions. I shall endeavor to show that the evidence obtained by our diagnostic methods can often offer a valuable guide for treatment.

There is abundant evidence at the present time that the endocrine glands have a profound effect on the living processes. Even our modern knowledge of the physiology of the endocrine glands is comparatively meager. Nevertheless it has brought out their following salient functions:

1. They regulate growth and development.
2. They regulate metabolism.
3. They sensitize the peripheral and central nervous systems.

Even a cursory examination of the essential symptoms of the evident endocrine syndromes reveals disturbances in growth and development which loudly proclaim this regulating function of the gland involved.

The characteristic changes in the features and the abnormal configuration of the bones in acromegaly leave no doubt as to the function which the pituitary gland has of regulating the growth and development. The short stature and the childlike mentality

[1] From the Department of Endocrine Diseases.

of the cretin are easily recognized manifestations of deficient thyroid secretion.

The effect of the endocrine glands on metabolism is also apparent in the well-defined endocrine lesions. In exophthalmic goiter the loss of weight is characteristic, while fat pads and obesity accompany myxedema. And the hyperglycemia, the glycosuria, and loss in weight are well-known manifestations of pancreatic diabetes. In Addison's disease, too, the profound weakness may be secondary to the associated hypoglycemia.

The effect of the endocrine glands on the peripheral nervous system is easily recognized. The tendency to perspiration and the tremor which is present in certain types of exophthalmic goiter speak for an effect on the peripheral nervous system, and the cyanosis and other signs of hypo-adrenalism also indicate a disturbance of the peripheral nervous system.

There are other effects produced by the endocrine glands that have not yet been definitely established, but which cumulative evidence is gradually establishing as facts. The resistance and the inherent susceptibility to infections seem to be bound up with the functions of the glands for internal secretion. Indeed, even the characteristics of personality seem to be determined by the gland which has the preponderating function in the individual.

In the study of the emotions and their relation to endocrine conditions Cannon has shown that certain fundamental emotions—which were the only ones that he could study in the laboratory—are associated with increased secretion of the endocrine glands. Of course, the great question that Cannon's conclusion has brought forth is whether the endocrine secretion is the cause of the emotion or whether the emotion is the cause of the secretion. From a clinical standpoint, however, the assumption that the endocrine secretion is the cause of the emotional and nervous phenomena is of great practical and therapeutic value.

The diagnosis of endocrine disturbances would be simple indeed if we possessed quantitative methods for detecting the presence in the blood of the specific secretion of each gland, or if we could recognize the absence of any specific endocrine substance. Unfortunately, however, this is still a vision of the

distant future. Consequently, we must depend upon clinical methods and indirect tests for the diagnosis of endocrine disturbances.

The clinical method has proved to be very valuable, but it requires much closer and more careful clinical observation than has heretofore been practised in our physical examination. The clinical methods used in the diagnosis of endocrine lesions are based upon the fact that we are able to recognize certain gross disturbances in the function of certain endocrine glands by the occurrence of definite clinical syndromes. Consequently, the presence of the same symptoms in a lesser degree are useful in determining a disturbance of the same endocrine gland when a gross lesion is not apparent. In a similar manner the presence of these same symptoms in any disease enables us to establish an endocrine basis for that disease. For example, exophthalmic goiter is regularly characterized by the production of exophthalmos, tremor, tachycardia, von Graefe and Stelwag signs. Consequently, it is a reasonable assumption that one or several of these symptoms—in the absence of any other definite cause—should be considered as stigmata of excessive secretion of the thyroid gland. Or, since Addison's disease is characterized by pigmentation, low blood-pressure, hypoglycemia, and general and profound asthenia, it is reasonable to assume that these symptoms—when they occur without other definite cause—are stigmata of deficient adrenalin secretion. We can, therefore, classify the endocrine stigmata in the following way:

1. Thyroid stigmata: (*a*) hyperfunction,
   (*b*) hypofunction.
2. Adrenalin stigmata: (*a*) hyperfunction,
   (*b*) hypofunction.
3. Pituitary stigmata: (*a*) hyperfunction,
   (*b*) hypofunction.
4. Thymus stigmata.
5. Pancreatic stimgata.
6. Gonadal stigmata.

The stigmata are the symptoms of the definite syndromes produced by gross lesions of the various endocrine lesions.

Furthermore, since the endocrines regulate growth and development, we may utilize disturbances in growth and development as a means of recognizing disturbances in the endocrine glands. For example, since certain bony changes occur in pituitary disturbances, the presence of these characteristic bony changes should lead us to assume a lesion of the pituitary gland.

It is recognized that the endocrine glands regulate metabolism; consequently, we may be permitted to assume an endocrine disturbance when certain characteristic metabolic disturbances are present.

Since we have evidence that the endocrine glands sensitize the peripheral and central nervous systems, the presence of defective function in the peripheral or central nervous systems should lead us to deduce a deficient sensitization, and consequently a deficient secretion of one or several of the endocrine glands. For example, we know that the adrenal secretion is the great sensitizer of the sympathetic nervous system. When, therefore, we have evidence of a highly sensitized sympathetic nervous system which is manifested clinically by a characteristic group of symptoms known as the state of sympathicotonia, we have good reason to assume that this state is due to an excessive secretion of the adrenal gland. Furthermore, we can utilize this fact to establish an indirect test for the presence, in a rather gross way, of the excess or diminution of the adrenal secretion.

We know very definitely the pharmacologic effect of adrenalin. We know also that these effects are due to peripheral sympathetic stimulation. Consequently, if the injection of the usual dose of adrenalin chlorid shows the patient to be unusually susceptible to adrenalin, or if a smaller dose produces marked effects, it is a reasonable assumption that this effect is due to the presence in the system of an excessive amount of the adrenal secretion.

On the other hand, it has been shown by Eppinger and Hess and others that certain individuals suffer from a group of symptoms which are the result of excessive peripheral sensitization of autonomic, vegetative, or so-called vagotonic system, because the vagus nerve and its branches is the most important

nerve of this group. The nerves constituting this system are all efferent nerves and consist of the following nerves:

1. Oculomotor, innervating the muscle of accommodation and the muscles for contraction of the pupil.
2. Glossopharyngeal.
3. The vagus nerve, innervating the blood-vessels, the mucous membranes of the mouth, throat, and nose, the salivary glands, the trachea, the bronchi, the digestive tract, the liver, the bile-ducts, the pancreas and its ducts, the blood-vessels, the kidneys, the pelvic organs, and the genito-urinary tract.

The symptoms which are produced by a state of increased sensitization of the autonomic or vagotonic nervous system are the following, and the syndrome formed by these symptoms is called the state of *vagotonia:*

1. Contracted pupils.
2. Stelwag sign.
3. Von Graefe's sign.
4. Excessive secretion of tears.
5. Hot flushes.
6. Excessive salivation.
7. Excessive perspiration.
8. Slow heart-beat and paroxysmal attacks of rapid heart-beat.
9. Low blood-pressure.
10. Attacks of bronchial asthma.
11. Eosinophilia and lymphocytosis.
12. Globus hystericus.
13. Gastric pains with hyperacidity.
14. Pylorospasm and cardiospasm.
15. Mucous colitis.
16. Spasm on urination.
17. Tendency to erections.

It is generally believed that the clinical state of vagotonia is definitely associated with a disturbance of one or several of the endocrine glands, although which gland is disturbed is not established, but the probabilities point to the thyroid and thymus. It is therefore reasonable to assume that if a patient has vagotonic

symptoms, these symptoms are an indication of the disturbance of these endocrine glands. We know also that we can produce vagotonia artificially by the injection of pilocarpin; consequently, if the injection of the usual dose of pilocarpin produces profound vagotonic symptoms, or if a patient is so susceptible to pilocarpin that a very small dose produces an unusually profound effect, we can deduce from this effect the fact that the patient is suffering from an endocrine disturbance characterized by vagotonia.

Eppinger and Hess have classified individuals into vagotonics or sympathicotonics, according to whether they show stigmata of the autonomic or sympathetic nervous system. Subsequent work, however, shows that certain individuals show stigmata of both systems. Furthermore, the individual who shows vagotonic stigmata at one time may subsequently show sympathicotonic stigmata. But since these constitutional manifestations are evidence of an endocrine disturbance, and since we know that endocrine disturbances are dynamic and characterized by compensatory phenomena, the change of a vagotonic individual into a sympathicotonic one is merely an indication of compensation of the reciprocal gland.

This afternoon I shall emphasize particularly the diagnostic value of the vagotonic and sympathicotonic tests and attempt to show that the information thus obtained can often be utilized in a practical and therapeutic way. Of course, I realize that at times these facts do not hold good, because in endocrine conditions we are still only on the outskirts of a tremendously fertile and prolific field for brilliant research, and only a very few definite axioms have as yet been established from which to draw absolutely reliable conclusions. Consequently, whatever facts are established in endocrinology at the present time must be modified by the coefficient of its pioneer state.

In the normal individual there is a constant balance between the autonomic or vagotonic and sympathetic systems. In other individuals a disturbance in this balance is disturbed, and the disturbance manifests itself by the presence of vagotonic or sympathicotonic symptoms, and therefore increased susceptibil-

ity to pilocarpin in the former and increased susceptibility to adrenalin in the latter group of symptoms.

Since we have shown that both of these states are manifestations of the functions of some of the endocrine glands, when one or the other of these states predominates we can deduce an endocrine disturbance. Consequently, until we have more definite methods, by treating the evident excesses of the state of vagotonia or sympathicotonia we can symptomatically improve and often cure many of these endocrine manifestations. For example, we know that cases of exophthalmic goiter may be divided into several groups. The usual case gives evidence, both in its clinical phenomena and in the pharmacologic tests, of both sympathicotonia and vagotonia. On the other hand, some of these cases show evidence only of sympathicotonia and give a marked adrenalin reaction. It is quite possible that in these cases the sympathicotonic manifestations are due to the adrenal gland. There is also a third, though a rarer, group of exophthalmic goiters which shows only vagotonic symptoms and gives a marked pilocarpin reaction. These cases are believed to be accompanied by an enlarged thymus gland. When, therefore, we have established that the case of exophthalmic goiter in question is one with marked sympathicotonic symptoms, we may treat that case by attempting to lessen the sympathicotonia. We cannot as yet obtain any endocrine substances that are sympathetic depressants; consequently, we must resort to an indirect method to lessen the sympathicotonia. This can be done by producing an exaggerated state of vagotonia by the administration of pilocarpin, thus producing an overbalance of vagotonia to neutralize the sympathicotonia, since in the normal individual a balance between these two states is present.

On the other hand, a case of exophthalmic goiter with vagotonia may be treated in two ways: (1) By directly lessening the sympathicotonic with atropin; or (2) by producing a state of sympathicotonia with adrenalin, or by both methods. In a similar manner we may utilize the same method with other disturbances of any of the other endocrine glands.

Another method of treating endocrine lesions is by taking

advantage of the fact that when an excessive or deficient function of one gland is accompanied by a deficient or excessive function of another, the feeding of the reciprocal gland will often improve the disturbance in the affected one. For example, we know that hyperthyroidism is very commonly accompanied by an excessive secretion of the pituitary gland. Consequently, the feeding of pituitary gland will often help cases of exophthalmic goiter.

A third method for treating endocrine disturbances consists of taking advantage of the fact that certain individuals can be classified according to the gland which has the predominating secretion in them or according to whether they manifest sympathicotonic or vagotonic signs. This may be determined by a study of the personality of the individual, his activities, his likes and dislikes, his susceptibility to various diseases, and the presence or absence of various endocrine stigmata, as well as vagotonic or sympathicotonic signs. Such an individual may suffer from certain symptoms resulting from a sudden loss of this predominating secretion.

The following group of cases indicate particularly the value of the vagotonic and sympathicotonic tests as an aid in diagnosis and treatment. I have particularly chosen cases with definite endocrine lesions to emphasize these conditions. By the presence of the characteristic endocrine stigmata and the determination of the vagotonic or sympathicotonic state in an individual with an endocrine disturbance, but no apparent lesion, we can establish with a fair degree of accuracy which gland is involved, and we can treat the case according to the evidence thus obtained.

CASE I. **Hyperthyroidism with Sympathicotonia.**—A. D., a young Irish maid thirty years of age, came to the clinic complaining that for the last few months she had noticed a small lump in the lower part of the neck about the size of a cent. This lump gradually grew larger, until at the present time it is the size of a half-dollar. In rainy weather this lump becomes larger and she feels as if it were pressing on her throat. This usually lasts a day and then gradually passes away. For the last month she

has had throbbing of the heart and becomes very easily excited. She has noticed that her eyes have become more prominent. She sleeps very well and otherwise feels perfectly normal. She has no cough, no expectoration, no pain in the chest; does not catch cold easily. She has slight dyspnea on exertion, at which times she has palpitation of the heart. Her appetite is good; bowels regular; has vomited occasionally. She does not perspire even in hot weather.

She had measles at the age of seven, not followed by any sequelæ; no other children's diseases. She has always been strong and healthy. Her menstruation has always been regular and is usually of the twenty-eight-day type. Her mother died at the age of sixty-four from an unknown cause; her father is still living and well. She had one living sister who is well. One brother died in infancy from an unknown cause. There is no history of tuberculosis, rheumatism, cancer, or cardiovascular disease in the family.

The patient is a rather short, highly excitable young woman. There is no rash on the skin, but the skin is dry. The hair is abundant and glossy. There is no evidence of any general glandular enlargement. The nose and ears show no evidence of any abnormal changes. There is considerable exophthalmos of both eyes, and the eyes are bright and glistening, with positive Stelwag and Von Graefe and Möbius signs. The pupils are round, equal, and they react to light and accommodation. The teeth are in good condition; the tonsils are congested, but are otherwise normal.

There is a small nodular mass in the middle of the thyroid about the size of a ping-pong ball, which, however, is not tender, and no thrills can be felt over the thyroid. No cervical glands can be felt. The chest is normal in shape and contour, and the expansion is good. The lungs reveal no physical signs of any abnormal changes. The heart is enlarged, the left border extending about 5 inches to the left of the median line; the sounds are regular, of good force and muscular quality. There is a loud blowing systolic murmur heard at the apex and transmitted afterward to the aortic area and to the left axilla.

The abdomen is normal in shape and contour; there are no areas of tenderness, abnormal rigidity, abnormal masses, or free fluid. The liver and spleen are not enlarged. The kidneys are not palpable. The extremities show only a fine tremor in both hands; there is no edema in the lower extremities. The reflexes are all active.

The urinary output is within normal limits, and the urine has a specific gravity of 1020; is acid in reaction and contains no sugar or albumin, and microscopically only a few white blood-cells.

The blood examination showed red blood-cells 4,800,000; hemoglobin, 85 per cent.; white blood-cells, 9000; polynuclears, 68 per cent.; lymphocytes, 32 per cent.; eosinophils, 1 per cent.; basophils, 1 per cent.

The roentgenogram of chest showed a small goiter in neck extending below the sternum, but the thymus was not enlarged.

The injection intramuscularly of 1 c.c. of adrenalin chlorid, 1 : 1000 solution, produced a marked exaggeration of the tremor; the patient became very excitable and nervous. The blood-pressure rose from 144 systolic to 160, and diastolic, from 100 to 110, in half an hour. The blood-sugar rose from 0.14 to 0.28; the nervous phenomena were markedly increased.

The injection of $\frac{1}{20}$ gr. of pilocarpin hydrochlorid two days later produced no change in the pulse-rate, no change in the blood-pressure; only very slight sweating, and a secretion of only 5 c.c. of saliva in one hour.

It is quite evident that we are dealing here with a case of exophthalmic goiter showing evidence of a sympathicotonia, but no evidence of vagotonia. The fact that a sympathicotonia was present gave us the guide to treatment. The patient was put on pituitary extract, whole gland, 0.15 gm., three times a day, with pilocarpin hydrochlorid, gr. $\frac{1}{20}$, three times a day. This was followed by almost immediate improvement. The tachycardia is greatly improved, the pulse-rate changing from 120 to about 90. The tremor has disappeared; the exophthalmos has diminished, and at the present time—which is four months from the first observation—the enlargement of the thyroid has diminished to about half its former size.

A word as to the rationale of the treatment. The pituitary gland feeding was given on the basis of the fact that hypersecretion of the thyroid is accompanied by deficient secretion of the pituitary; consequently, overfeeding of pituitary tends to neutralize the excessive secretion of the thyroid. Furthermore, we had evidence of a sympathicotonia. In other words, the thyroid—or possibly the adrenal—was secreting a substance which produced a sympathicotonia. There is no glandular substance that we know of at present that acts as a sympathetic depressant. But since in normal conditions there is a balance between sympathicotonia and vagotonia we attempted to overcome the sympathicotonia by increasing the vagotonia, which we accomplish by means of pilocarpin, the best vagotonic stimulant. Furthermore, we had evidence in the effect of our pilocarpin tests of a deficient vagotonia.

CASE II. **Case of Exophthalmic Goiter, with Vagotonia and Gastric Symptoms.**—The patient, S. P., a woman of twenty-seven, came to the clinic complaining of pain in the epigastrium and vaginal discharge for the last three years. The illness began about three years ago, with pain in the epigastric region which radiated around both sides of the abdomen. At the same time she noticed that her thyroid gland became more prominent, and it has gradually grown larger. She stated that she felt as if a belt were tightening about her waist, and at times the pain was so severe that she had to double up to relieve it. The attacks lasted for from a few hours to three or four days—usually for about half an hour to an hour. The pain is intermittent in character, and nothing relieves it. She has always been a neurotic woman and perspired freely on the slightest exertion, and suffers from palpitation of the heart.

She has had a whitish or yellowish-creamy discharge from the vagina for the last eight years, which has recently improved and is now of a watery character. She has a burning sensation on urination at times. For the past two years she has been extremely dizzy.

She had measles at the age of six, but no sequelæ, and has

never been ill since. Her husband has lues and is now being treated with mercury and salvarsan injections. She has had a Wassermann taken, which was weakly positive. She has had twelve mercury injections.

Her father is living and well; her mother died of cardiac disease; she has a brother and sister, both living and well.

The patient is a rather thin, emotional young woman who is fairly comfortable. There is no rash on her skin, but red blotches appear on the skin on the slightest touch, and the axillæ become covered with profuse perspiration. No evidence of any general glandular enlargement. The pupils of the eyes are contracted, round, and equal, but they react very slowly to accommodation and very slightly to light; there is a Von Graefe and Stelwag sign. There is a slight exophthalmos. The nose and ears show no evidence of any abnormal changes. The teeth are in good condition and the palate is highly arched; the tonsils are not enlarged. There is a slight congestion of the throat. In the neck there is a moderate enlargement of the thyroid gland, but no thrill is felt over it. The chest is normal in shape and contour and the expansion is good. The heart is not enlarged. The sounds are regular, of good force and muscular quality; no murmurs are heard. The pulse is regular and of good volume; its rate is 60, but the rate changes quickly.

The systolic blood-pressure is 98; diastolic, 66. There is no evidence of thickening in the palpable vessels. The abdomen is not distended; there are no areas of tenderness, abnormal rigidity, or masses to be felt. The liver and spleen are not enlarged. There is considerable tenderness on pressure in the epigastrium. The kidneys are not palpable; the stomach is not dilated.

The extremities are not edematous or tender. The knee-jerks are very active.

Laboratory Findings.—The urinary output was within normal limits, the urine had a specific gravity of 1018; it was acid in reaction; it contained no albumin, no sugar, and microscopically there were no casts, but many W. B. C. present.

The gastric analysis after an Ewald test-meal showed free

HCl 50. Total acidity 82; no lactic acid, considerable mucus, and microscopically some starch granules and undigested food particles. The blood count showed B. B. C., 4,500,000; hemoglobin, 85 per cent.; W. B. C., 8000; polynuclears, 65 per cent.; lymphocytes, 33 per cent.; eosinophils, 2 per cent.

Examination of the nervous system shows no areas of anesthesia; no Rhomberg; no ataxia; no paralysis; no involvement of any of the cranial nerves; no Kernig or rigidity of the neck; no Babinski. The only positive signs of the nervous system are the pupillary disturbance already referred to and the exaggerated knee-jerks.

The injection of 1 c.c. of adrenalin hydrochlorid, 1 : 1000 solution, intramuscularly, caused only slight change in the blood-pressure—from 98 to 102 in the systolic, and from 66 to 68 in the diastolic. No tremor was produced and no nervous symptoms. The pulse-rate, however, changed from 88 to 92, and the blood-sugar from 0.144 to 0.150. The injection of $\frac{1}{10}$ gr. of pilocarpin hydrochlorid, however, produced a marked effect. The pulse-rate changed from 88 to 120. The blood-pressure remained the same, although it went up a few points in the first ten minutes after the injection. There was marked perspiration all over the body; and there was a secretion of 165 c.c. of saliva in a half-hour.

This case gives evidence of a moderately enlarged goiter with symptoms of vagotonia. In addition, there is a history of syphilis in the husband, and there is evidence of pupillary disturbance and exaggerated knee-jerks. The problem, however, is whether the patient is suffering from a gastric crisis as part of a cerebrospinal lues, or whether it is hyperthyroidism with vagotonia.

At any rate, there is evidence of a very marked vagotonia, and while we cannot definitely decide whether the hyperthyroidism of the cerebrospinal lues is responsible for the condition of vagotonia, nevertheless we used the vagotonia as a guide for endocrine treatment. The patient was put on pituitary extract, 0.15 gm. three times a day, so as to lessen the hyperthyroidism symptoms; and was given atropin sulphate, $\frac{1}{200}$ gr., to lessen the vagotonia. She came back about two weeks later, stating that the epigastric pains had gradually subsided and that she had not had any at-

tacks for some time. She is still under observation, though she has been free from attacks ever since the beginning of the treatment, about three months ago.

CASE III. **Subthyroidism with Adrenal Insufficiency.**—M. B., aged forty-one, was referred for diagnosis in July, complaining of pains in the back and extremities. The illness began about two years ago with pains in the neck, spine, and lumbosacral region, which persisted for a year. At that time she went to a gynecologist who performed a hysterectomy for these symptoms. The operation, however, did not relieve the symptoms, but the pains extended to the arms and legs. The pains seemed to be localized to the muscles.

A short time after the onset of the illness epigastric pains developed, and about September, 1918, she began to notice puffiness of the face and eyelids which has persisted ever since. A similar puffiness of the ankles has gradually developed in the last few months. The patient has had occipital headache ever since the onset, and she has also noticed that her skin was dry and scaly, and she rarely perspired even in the very hottest weather. She complains particularly of extreme fatigue, which is so bad that she can rarely get out of bed. She is always drowsy and stuporous. She suffers from stubborn constipation. Her nose is frequently stuffed so that she cannot breathe, and she has now become a mouth-breather on that account.

She had the usual illnesses of childhood and an attack of rheumatism twelve years ago which lasted seven months. She has been married eighteen years, has had two children, and has had four miscarriages, occurring after the birth of the last child. The family history is negative. There is nothing in her habits that is at all relevant to her condition.

Mrs. B. presents the appearance of a rather obese, stuporous, middle-aged woman. There is no rash on the skin, but there is a chocolate-colored spot about the size of a 25-cent coin on the extensor surface of each arm near the elbow-joint. The skin of the entire body is dry, waxy, and scaly. There is no evidence of any glandular enlargement. The scalp is covered with an abun-

dance of thick, dry, coarse hair. The face is puffy, especially around the eyelids. The eyebrows are normal in size, but not bushy. The eyes are dull and lusterless and the pupils of the eyes are round, equal, they react to light and accommodation, and there is no nystagmus. The nose and ears show no evidence of any abnormal lesions. In the mouth the teeth are in fairly good condition, they are not loose and there is no purulent secretion from their sockets; the throat is congested; the tonsils are small and submerged and no purulent pockets are seen, nor can pus be expressed from the follicles. In the neck the thyroid gland is barely palpable and no cervical glands are to be felt. The chest is normal in shape and contour and the expansion is good. The lungs give no evidence of pathologic changes. The heart is not enlarged, the sounds are regular, rhythmic, of good force and muscular quality, and no murmurs are heard. Moderate exercise causes only a rise of ten beats in the pulse-rate and does not produce any murmurs. The pulse is regular, of good volume, and there is no evidence of arteriosclerosis in the palpable vessels. The systolic blood-pressure is 110, diastolic 90. The abdomen is not distended and there are no signs of fluid or abnormal masses felt. The liver and spleen are not enlarged and the kidneys are not palpable. There is considerable tenderness on pressure at the lumbosacral junction, and on either side of this region a number of small fatty nodules are felt. The rest of the spine is not tender even on extensive passive motion. The lower extremities show only a slight edema of the skin over the tibiæ.

Examination of the nervous system shows no evidence of a lesion in any of the cranial nerves, no areas of anesthesia, and no paralyses. The superficial and deep reflexes are all normal. There is marked tenderness on pressure along the muscles of both upper and lower extremities.

Vaginal examination shows only a stump of cervix; the body of the uterus and the adnexa cannot be felt.

Rectal examination gives no positive findings other than a few hemorrhoidal tabs.

The urinary output in twenty-four hours is within normal limits. The urine is cloudy and acid in reaction; specific gravity

1006 and 1024; no albumin, no sugar, no casts, and only a few epithelial cells on microscopic examination. The feces showed no parasites nor any blood either by chemical or microscopic examination. The gastric analysis after an Ewald test-meal showed free HCl 30, total acidity 90, no lactic acid, a faint trace of blood by the guaiac test, a few yeast cells and food particles on microscopic examination. Examination of the blood showed R. B. C. 3,800,000, hemoglobin 80 per cent., white blood-cells 9000, polymorphonuclears 46 per cent., lymphocytes 56 per cent., and no eosinophils. The Wassermann reaction was negative.

The pilocarpin test for vagotonia showed the following drop in the blood-pressure in forty-five minutes: Systolic, from 110 to 105; diastolic, from 90 to 80. The pulse-rate remained the same, there was no sweating produced, but the patient secreted 20 c.c. of saliva in forty-five minutes.

The adrenalin test for sympathicotonia showed no change whatever in blood-pressure or pulse-rate, there was no glycosuria, and the blood-sugar was changed from 0.12 to 0.14.

The conclusion from these two tests seems to indicate a deficient vagotonia with a markedly deficient sympathicotonia.

The positive findings of this case are the following:

1. The mental torpor and drowsiness.
2. The moderate obesity.
3. The tenderness at the lumbosacral junction.
4. The tenderness along the muscles of the extremities.
5. The dry, scaly, waxy skin.
6. The edema and puffiness of the face and slightly around the tibiæ.
7. The lymphocytosis.
8. The evidence of deficient vagotonia and sympathocotonia.
9. The low blood-pressure.

The patient was originally sent for an explanation of the edema, which, of course, suggested nephritis or trichinosis. The negative urine examination and the low blood-pressure eliminate chronic nephritis. The absence of eosinophilia as well as the absence of a history of having eaten pork eliminate trichinosis. An endocrine disturbance is, of course, suggested by the marked

torpor, the drowsiness, the low blood-pressure, the persistent fatigue, the obesity, and the scaly, waxy, dry skin. These symptoms suggest a hypothyroid condition. The marked fatigue, the chocolate-colored spots on the arms, the tenderness along the skeletal muscles, the low blood-pressure, and the weakness and lethargic state suggest an adrenal deficiency. The pilocarpin test gives a practically negative reaction, indicating a deficient vagotonia. The adrenalin test indicates a deficient sympathicotonia.

It is interesting to correlate the clinical findings of an endocrine disturbance with the pharmacologic evidence of an endocrine deficiency. The adrenalin test suggested the disturbance in the adrenal gland. The negative tests indicated that there is such a deficiency of adrenal secretion in the blood, since the injection of 1 c.c. of adrenalin did not produce even a normal reaction. Although there is clinical evidence of a distinct submyxedema, we cannot localize definitely at the present time the gland or glands which produce the state of vagotonia, although it seems that the thymus, thyroid, and the lympathic system are the sources for autonomic sensitizers. We cannot say whether there is any relationship between the absence of vagotonia and the submyxedema, but there is no evidence of a large thymus or a lymphatic diathesis, although the blood count shows 56 per cent. lymphocytes.

Treatment.—The patient was put on thyroid feeding, beginning with gr. $\frac{1}{10}$ t. i. d., which was gradually increased in the course of a few weeks to gr. 1 three times a day. Within two weeks after treatment was begun the puffiness of the face and the edema entirely disappeared, the drowsiness was changed to alertness, and the patient felt almost well. The pains disappeared in a week after treatment was begun. When the larger doses of thyroid were reached the pains returned, although the symptoms of submyxedema had disappeared. The pains and weakness had markedly improved for almost a week after the injection of pilocarpin hydrochlorid, gr. $\frac{1}{10}$, given for diagnostic purposes. Subsequently we modified the treatment by adding gr. $\frac{1}{20}$ of pilocarpin hydrochlorid and resumed the thyroid, gr. $\frac{1}{10}$ to $\frac{1}{8}$,

and adrenal extract, gr. $\frac{1}{15}$ doses, with the pilocarpin. This relieved the pains which were the only remnants of the original symptoms present, the subthyroid symptoms having been relieved by the administration of thyroid. The rationale for the use of adrenal extract was indicated by the evidence of adrenal insufficiency, and the rationale for the use of pilocarpin was indicated by the fact that the pilocarpin test was only very slightly positive.

The treatment of this case is interesting because it illustrates the value of the vagotonic and sympathicotonic tests from a therapeutic standpoint. While the vagotonic test does not always localize the lesion, yet pharmacologic evidence of diminished vagotonia indicates that the production of a vagotonia will improve many of the symptoms due to the apparent endocrine disturbance, although the gland affected cannot always be localized.

CASE IV.—**Case of Neurasthenia with Evidence of Sympathicotonia and Hyperthyroidism.**—B. G. was admitted to the Lenox Hill Hospital complaining of weakness and fainting spells during the past year. She has had these fainting spells and palpitation of the heart and has been extremely nervous. She has had burning pains in the stomach, eructations of sour material in the throat, and, at times, belching of gas. She has lost 15 pounds in weight during this time. In fact, close questioning revealed that she suffered from all the characteristic symptoms of the typical neurasthenic.

She had the usual infections of childhood, and had typhoid fever twelve years ago; otherwise her history has been negative. Her menstruation began at the age of thirteen, was regular every twenty-eight days, and lasted for three to four days. She has been married fifteen years and has four children. She has never had any miscarriages. Her father died of apoplexy.

The history is very indefinite, and seems to be that of general asthenia. The patient is a poorly nourished, thin, middle-aged woman, who is highly excitable and extremely nervous. There is no rash on the skin, but there is a brownish pigmentation over the front of the chest and the upper part of the back, which is ap-

parently a chromophytosis. There is no general glandular enlargement.

The pupils of the eyes are round, wide, and react to light and accommodation. There is no exophthalmos, and no Stelwag, Von Graefe, or Möbius sign. The nose and ears are apparently normal. The teeth are in good condition; the throat is slightly congested. There is a slight enlargement of the thyroid gland, but it is not tender nor are thrills felt over it. There are no palpable cervical glands. The chest is normal in shape and contour. The lungs are normal; the heart is not enlarged; the sounds are regular, rhythmic, and of good quality, and no murmurs can be heard. The pulse is rapid—about 80 to 90. The blood-pressure is 140 systolic and 100 diastolic. There is a slight thickening of the palpable vessels.

The abdomen is scaphoid in contour; there is tenderness on pressure in both inguinal regions, but no evidence of free fluid or any abnormal masses. The liver border may be felt one finger-breadth below the costal margin, but the spleen is not enlarged.

There is a fine tremor in both hands, but otherwise both upper and lower extremities are normal, and the knee-jerks are active. Vaginal examination is negative. The daily urinary output was within normal limits; the urine was acid in reaction, with a specific gravity of 1031, a faint trace of albumin, no sugar, and a few leukocytes on microscopic examination.

The blood examination showed a negative Wassermann. The blood-count showed red blood-cells, 5,200, 000; hemoglobin about 80 per cent.; white blood-cells, 7400; polynuclears, 68 per cent.; lymphocytes, 29; eosinophils, 1 per cent.; mononuclears, 7 per cent.

x-Ray examination of the chest showed no thymus enlargement. The injection of 1 c.c. of a 1 : 1000 solution of adrenalin chlorid intramuscularly produced a tremendous reaction, the patient began to tremble all over. There was a rise in the blood-pressure—systolic 30 points, diastolic 20 points—and the patient seemed to be in a profound shock. In other words, we had a marked effect of sympathicotonia. A pilocarpin injection, gr. $\frac{1}{10}$, given a few days later was practically negative. No change

was produced in the pulse-rate, the blood-pressure, or the secretion of saliva.

A blood-sugar test could not be done on account of the patient's objection to the removal of blood from the vein.

This was evidently a case of marked neurasthenia with signs of profound sympathicotonia. From the fact that there was a slight enlargement of the thyroid, it seemed very likely that the thyroid was responsible for the sympathicotonia. An injection of gr. $\frac{1}{300}$ of atropin sulphate caused profound toxic symptoms which resembled the effect of the injection of adrenalin.

We explain this by the fact that the atropin paralyzed the vagotonic system so as to give freer play to the already overactive sympathetic. The patient was put upon pituitary extract, whole lobe, to overcome the hyperthyroidism, and pilocarpin hydrochlorid, $\frac{1}{20}$ gr., three times a day, to produce a vagotonia and thus establish a better balance between sympathicotonia and vagotonia. She was seen again about a month after her discharge from the hospital, and her nervous symptoms had markedly improved.

It is interesting to note also that at the last observation—which was about five months after her admission to the hospital—the patient was entirely free from all symptoms. She is now three months pregnant, and states that for the last two months her symptoms have completely disappeared, in spite of not taking any treatment.

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PHYSICAL THERAPY IN LOCOMOTOR ATAXIA

Cause of Disease Definitely Established. Therapy of the Disease Still a Matter of Controversy. Physical Therapy as a Means of Relief of Various Symptoms. Methods of Its Application.

LOCOMOTOR ataxia is a syphilitic affection of the central nervous system. The symptoms are due to an invasion of the nervous structures by the Spirochæta pallida and the subsequent destruction of the nervous tissues.

I place these facts at the beginning of this paper with the intention to pour a little cold water on the enthusiasm of some physical therapist who claimed or claims great results in the treatment of locomotor ataxia by these methods. All we can attain is an alleviation of one or the other symptom, a more or less strong suggestive influence which may sometimes have a very marked effect.

I shall in the course of this paper, when I speak of Maloney's ideas on this subject, refer again to the mechanism of action of physical therapeutics.

The old principle of medicine, the *primum not nocere*, must be foremost in our minds when we deal with a tabetic, because few other patients can be so easily harmed as the tabetics.

Edinger has first formed the conception of the "Aufbrauchskrankheiten" of pathologic conditions in which the exhaustion of the structures is more rapid than the reconstruction. Tabes is one of these diseases, and our effort must always tend to the direction to diminish the exhaustion and to further the building up of the tissues.

This point of view must be dominant, and every procedure we wish to apply must first be scrutinized from this standpoint.

It is a well-established fact that stimulation increases the oxidation and the metabolism in the tissues. Under normal conditions this will tend to use up tissues which are in the process of dissolution and to stimulate those which are growing. In such disease, however, where the ratio between destruction and reconstruction is an unfavorable one for the individual, a severe stimulation will naturally do more harm than good, as the thorough destruction will be much more extensive than the possibility of reconstruction. In fact, it is possible that an overstimulation will change reconstruction into destruction.

Hydrotherapy is a method of treatment which has a wide range of possibilities. It is a sedative or a strong stimulus, depending on the form of application, temperature of the water, and the mechanical factor, for instance, water pressure.

Cold applications, particularly when combined with pressure, are a very powerful stimulus, and there is no doubt in my mind that they are very harmful if applied to tabetics or paretics. I have seen blindness develop in a tabetic during a heroic hydriatic cure, and acute mania in a paretic who previously showed only neurasthenic symptoms and where paresis was hardly suspected.

My experience is sufficiently impressive to warn against all severe hydriatic treatments. Partial ablutions, a shallow (half) bath at 92° to 88° F., and carbonic acid baths may be used with some benefit.

If a tabetic suffers from a syphilitic affection of the cardiovascular system, treatments known as beneficial in such conditions may be used, but we always have to keep in mind whether the possible help is worth taking the chance, however slight.

In many books which deal with electrotherapy we will find various recommendations. Galvanic currents, high frequency in the form of application of the Oudin electrode (violet rays), or diathermia is recommended, and successes are reported. We have to accept these statements with the proverbial grain of salt and a benevolent smile. A symptom-complex which is so changing as the locomotor ataxia is the most fertile soil for the reveries of an enthusiast or fanatic.

As far as massage is concerned I believe that it is of some value if done in a gentle way. Heavy deep massage increases apparently the pain, which is annoying and troublesome.

Before I turn to the discussion of mechanotherapy I must first mention the work of Dr. W. J. Maloney on the subject of locomotor ataxia. In his writings, particularly in his book "Locomotor Ataxia"[1] (the most instructive and fundamental work ever written on the therapy of tabes), he explains the mode of working of the physical therapy as well as its limitations.

The most important result of his studies is the discovery of the importance of psychologic factors on the symptom-complex, and the fact that the condition of the mental state is so closely related to the symptoms due to structural changes that a deterioration of the mental state causes an aggravation of all the symptoms and vice versa, that an increase in the symptoms affects the mental state and produces a vicious circle.

These discoveries explain in a simple way why so many forms of physical therapy have gained an undeserved degree of popularity. If the treatment is sufficiently impressive and if the physician is sufficiently convinced of the value of the treatment and is able to inspire hope and confidence in the patient, any treatment may give more or less transitory relief or improve the symptoms.

What we have to keep in mind is that we should not for the sake of a temporary impression, suggestive influence, and passing improvement aggravate the structural changes. The wise and conscientious physician will weigh properly the pros and cons and will not try to force a treatment on his patient which will ultimately harm him.

The most important symptom of the tabes dorsalis or locomotor ataxia is the ataxia. A man may have pain—only he knows about it; he may have difficulty in urination, this is not characteristic. He may be so unfortunate as to lose his eyesight and become a blind man, but what stamps him before himself and before the world as a tabetic is the ataxia, and therefore

[1] New York, 1918.

there is no symptom which has such an overaweing importance as the disturbance of his walking.

We must give all the deserved credit to Frenkel and Goldscheider, who have tried to correct these symptoms and who have developed a method of cure.

Frenkel has published a book which, up to the publication of Maloney, was the standard work, and he is the founder of the mechanotherapy of locomotor ataxia of re-education. This system, however, has many faults. It is based on the assistance of the eyes. He tries to replace the natural control of movement by the control of the eye. The result is that the patients treated with this method, though they may be able to walk in the light, are more helpless than ever in the dark or under unusual conditions.

I have used this method for twenty years, but have never been fully satisfied with the results. They are not perfect, and in my experience never lasting.

Maloney has placed the mechanical treatment of tabes on a new, scientific basis. To be able to understand his method and use it with success, it is necessary to give an outline of the basic principles of his method.

Beaussart, Lavallee, Erb, Pierre Marie, Bernard, and others have reported groups of tabetics and paretics whose infections could be traced correspondingly to one source of infection. This proves that there exists a special strain of Spirochæta pallida which has a specific affinity to the central nervous system.

It has furthermore been proved that tabetics or paretics rarely show lesions of other tissues, like skin, mucous membranes, etc. By large statistics Maloney could show that adequate and intensive antisyphilitic treatment with salvarsan and mercury does not seem to prevent the development of syphilis of the nervous system.

Though some physicians claim that they have been able to arrest the progress of these diseases of the nervous system by a certain course of mixed treatments, including intravenous injections of salvarsan, the general opinion is that these remedies do not penetrate these tissues in sufficient concentration to be

effective. This gave rise to the recommendation of the intraspinal treatment.

Notwithstanding the fact that reliable men report the cure of tabetics, we may accept it as a general rule that tabes at present is not amenable to our treatments, and Maloney claims that this is due to the fact that in the general infection caused by the Spirochæta pallida the vegetative nervous system has suffered, or is congenitally too weak and that it does not produce sufficient defensive substances to combat the disease. This weakness of the vegetative nervous system is the basis of neurasthenia and the fertile soil for the development of tabes or paresis.

This idea plays a very important rôle in the entire system of treatment. As we are not able to remove the cause of the disease, we ought to try to prevent the consequences.

Maloney lays great stress on the treatment of the preatactic stage and deals, therefore, extensively with the conception of the syphilitic neurasthenic—a conception which is a new one and which forms the basis of every curative procedure.

"Although a virulent spirochete may bring tabes to anyone, a non-virulent may make the nervous indivudual a tabetic or paretic. As the nervous syphilitic is a potential tabetic, a potential general paretic, he of all neurasthenics imperatively requires unremitting care. Syphilitics often complain of irritability of the increasing readiness with which they experience fatigue of tumultuous and irregular heart actions, of lack of appetite, hyperacidity and nausea, and constipation punctuated by diarrhea. These symptoms, common to states of mental stress, are due to increased tone of the vagus, and may be alleviated by a drug which reduces vagal tone, such as atropin," Maloney, Locomotor Ataxia, 1918, p. 190.

The modern tendency to prevent the development of diseases rather than to cure them is the cornerstone of Maloney's treatment of the preatactic stage—the treatment of the syphilitic neurasthenic.

We have shown that the nervous system when attacked by the Spirochæta pallida, particularly in an individual whose vege-

tative nervous system is probably congenitally weak, shows an increased tendency to destruction of nervous tissues and a decreased ability to reconstruction. It is, therefore, vital that we try to bring about a proper, favorable ratio by diminishing the destruction as long as we are not able to increase the recuperating power.

It is our duty to teach the syphilitic neurasthenic what he should do and not encourage him to do as much as he can. An overexertion or mental stress which goes beyond the recuperating ability of such a patient must ultimately lead to a break-down, to locomotor ataxia, or general paresis. This is the reason why we should not overtreat the nervous syphilitic with heroic, strenuous methods of physical therapy. In this stage the general practitioner has the fate of the patient in his hands. It is unfortunate that the patients with whom we have to deal mostly are not the syphilitic neurasthenics, but the full-grown tabetic or general paretic.

While it was advisable, even necessary, to follow the above-described procedure, the reduction of mental stress when dealing with a neurasthenic becomes imperative in the care of a tabetic. As long as we allow these patients to continue their mode of living, to use up and waste their energies in pursuance of their former duties, we may just as well not treat them at all. It would be just as well to allow a man who is suffering from lead-poisoning to continue in his occupation without proper warning and protection. We must not allow a letter-carrier to keep on walking all day, or the sportsman to ride on horseback, play tennis in tournament, or the business man to stay at his desk all day. We cannot expect to correct in a few hours the harm which is done in the rest of the day. There is no rule which applies to each patient. It depends on the tact and the good judgment of the physician as to what he may allow the patient to do or what he may forbid. The most important addition in the understanding of the symptom-complex of tabes and the most valuable suggestion for the treatment, which we owe to Maloney, is the realization of the importance of the psychologic factor.

It has been proved that the mental state has an equal part in the production of the symptom-complex of the tabes as the structural changes. A sudden shock, for instance, the realization that the patient is suffering from locomotor ataxia, may change the man who is merely complaining of pain into a helpless atactic. Overexertion, mental as well as physical, worry, and overtreatment have the same effect.

The tendency to become an ataxic is expressed mathematically by Maloney by the following equation:

$$\text{Coefficient of ataxia} = \begin{cases} \text{Ataxic tendencies.} \\ \text{Co-ordinating power.} \end{cases}$$

This means that the development of ataxia is not only dependent on the co-ordinating power, the structural changes, but on such conditions which disturb the mental equilibrium—worry, fear, and overwork.

We have, as shown above, no means to cure the structural changes to decrease the denominator, but we have the possibility to reduce the numerator—the ataxic tendencies. We can reduce it to such an extent that the coefficient of ataxia remains smaller than one (1), *i. e.*, the patient remains in the preataxic stage.

What I have said so far pertains mostly to the preataxic stage—a method to prevent ataxia. In a great many cases, however, we are called upon to treat the patients after ataxia is more or less fully developed. Our task then consists not only in preventive measures but in actual assistance. The treatment which Maloney recommends consists mainly in four methods, all of which, however, do not need to be used, depending on the condition of the patient.

These methods are: The treatment of the mental state; forced rest exercises; temporary mechanical support if needed; re-education.

I wish to say that I do not follow slavishly the recommendation of Maloney. The clinical picture of tabes is as variable as life itself. Each patient is a special study, and only those physicians will get good results who individualize the treatment

and adapt it to the needs of the case. My method of procedure is in some details different from his, but the treatment must be conducted on the basic principles as established by Maloney.

1. The staggering blow which the patient received when he heard the diagnosis, which in the mind of the laymen is a death sentence, must be counteracted by the reassurance that his condition is not hopeless, but will surely be cured. If the patient is unaware of the nature of his disease, one should not tell him the truth, or use a term which is recommended by Maloney —"syphilitic neuritis of the posterior roots." It is very unfortunate that it has become common knowledge that tabes is a syphilitic manifestation. To move about among his fellow-beings marked as a syphilitic is enough to disturb the mental equilibrium of any man.

Thus our principal task, before we commence an active treatment, is to re-establish hope in the mind of the disheartened, and to assure him that he will again become a useful member of society; also that he will be able to take care of his duties toward his family.

To accomplish it, it is advisable to remove the tabetic temporarily from his surroundings. It is clear that the depressing effect which is produced by his inability to attend to his social and vocational duties must work against a recovery. Isn't he confronted with his troubles daily? Doesn't he notice the reproachful attitude of his family, probably the reserve of his acquaintances? Doesn't he imagine that people talk about him and exaggerate it?

Everybody thinks locomotor ataxia incurable. What help is given to the patient when he returns improved and can show others that he is going to get well?

Most tabetics are depressed, morose, irritable, but otherwise mentally alert. In such cases where the mentality is somewhat affected a system of measuring his mental capacity has been used by Maloney—a system which is used in mental tests. By these tests the amount of deterioration can be measured, and by continuation of these exercises in conjunction with the treatment the progress in the improvement can be shown. I refer for the

details to Maloney's book, but omit it in this paper, as these methods are not essential for the treatment.

If we have gained the confidence of the patients, if we have been able to revive hope and to take the load off their minds, if we have succeeded in improving the mental state by relieving the mental stress, a great deal has been gained.

RELAXATION

The most valuable aid in obtaining this result is relaxation and the rest exercises. If I dwell longer than it seems necessary on this method, if I speak of its value in certain branches of human endeavor, though they do not belong, strictly speaking, to the treatment of tabetics, it is because I believe that relaxation is the foundation of every human accomplishment.

Some may claim that concentration is more important, but I believe that pure, strong concentration is only possible on the basis of relaxation. We have only a certain amount of energy at our disposal. If we want to concentrate our energies upon one task we must be able to relax in every other direction.

We remark how easy a certain man wins a race, but we do not stop to think why it is that this man does not break his own record. It is because he has concentrated all his energies in certain parts of his muscular system, leaving the others in as much a relaxed condition as feasible. This combination produces in the spectator the impression that the task was easily accomplished.

A good horseman sits lightly on his horse, his body is flexible, at ease, because he concentrates his energies on the adductor femoris and those muscles he needs for the control of the horse. The poor horseman sits on his horse like a clothes-pin.

If we try to remember a word, we are not successful as long as we try to force our mind. The tension of the mind brings about a tension in the muscular system. A complete relaxation will bring it back. The characteristic attitude of a poor singer is due to his exaggerated muscular actions. He stretches his arms, he raises himself on his feet as if he could pull the high tones out of his throat. If he could be taught to relax, and con-

centrate his energies on the muscle of his larynx his voice would gain in strength, in ease, and in volume.

I could multiply these examples by the score, but I would like to conclude my valuation of the relaxation by relating a case which was not a tabetic.

A young lady of thirty was sent to me for inability to walk. She was confined to her chair since seven years, and could only walk with crutches for a short distance and under evident effort. She had been under the care of a neurologist all this time. She showed no signs of spinal affection except a foot clonus on one side and highly exaggerated knee-jerks. I realized the functional character of her walk. Examination showed that she was unable to relax her muscles even when lying on the bed, and passive movements were very difficult to make. For years she was told that she could walk if she only wanted to, and all these years the poor girl tried with all her might, but the more she tried, the worse she got.

I started to relax her, taught her to let herself go even with the chance of falling, and to save her energies and try to get along at the expense of the least possible effort. I had the pleasure to see her improve gradually, and within two months' time she was perfectly well.

A tabetic whose sensory impulses are weak and delayed, and on that account misleading, does not trust them. He is in constant fear of falling, and tries to hold on anywhere he can. Fear is a poor guide for anybody. It is ruinous for the tabetic. Every muscle in his body is tense and so is his mind. He can't think of anything but falling and how to reach a goal safely. When he is used to the surroundings, and the fear subsides, then he will begin to move with comparative ease. Fear causes tensity of the muscles—tensity of muscles causes a waste of energy. The wasted ill-applied energy increases the fear. In a later chapter I shall show the importance of relaxation for re-education.

Maloney has recommended a certain system of rest or relaxation exercises. The relaxation thus accomplished is not merely impassivity of muscles, it is a voluntary action. Just as

we can be taught to contract a muscle, so can we learn to relax it voluntarily. The tabetic is involuntarily relaxed in sleep, but this is of no value. He must be taught to let his muscles loose at will.

A very good start can be taken by the breathing exercises. The patient lies on a couch or bed, which should be at least 3 feet wide, with slight support under his head in a darkened room, and blindfolded, to avoid every disturbance through the senses. He is told to take a deep breath—the form of breathing must be abdominal. It is advisable to put a sand-bag of about 2 pounds on his abdomen or exert some pressure with the hand to force his attention on the breathing. The breathing must be slow—about 12 a minute, and very deep. The patient is told to think of nothing else but the breathing. This is done twenty times. Then we let him breathe more and more shallow until he takes just as much air as he would in sleep—as much as he wants. He, however, must think of the breathing and nothing else. After a few minutes we resume the deep breathing, change to the shallow breathing, until the patient masters it. We find him asleep very often after a short sitting. The breathing exercises are followed by the relaxation exercises.

We generally begin with the muscles of the head and the neck. The posture of the head determines to a great extent the posture of the body, and the relaxation of these parts gains thus its importance. The patient closes his eyes and is told to let the eyelids droop without forcing the closure. The patient is further told to let the chin droop, and the operator tries by a gentle stroke of the facial muscles to relax them. We support the head with both hands, standing at the head of the bed, and try to move it passively forward and sideways, and turn it along its vertical axis. The slightest muscular action on the part of the patient can be easily noticed by the operator, and the patient should be told to stop it.

We then pass to the relaxation of the arms. The arm is supported by placing one hand under the lower third of the forearm and the middle of the upper arm and make rotary movements in the shoulder-joint trying to reach the limits of

motion. Off and on we let the arm drop on the bed. We put the arm above the head across the chest. We then loosen our hold on the forearm to let it fall, or raise it so that the elbow-joint is fully flexed; stretch it again and let it loose again. We do this in all the positions which can be taken in the shoulder-joint. By shaking the forearm slightly we can produce relaxation in the muscles which control the wrist, the hand, and the fingers. We ask the patient to play dead. Whenever we notice a resistance to the passive motion we draw the patient's attention to it with subdued voice. The patient should not answer, not even yes or no, nor nod consent.

Whenever we see that no progress is made we resume the breathing exercises, advising the patient to think of nothing else but the breathing. As the relaxation of one extremity facilitates the relaxation in his fellow, we go from the one to the other. After obtaining some results in the arms, we turn to the legs.

By supporting the calf and the thigh, we rotate in the hip-joint in all directions, withdrawing the support of the calf, while the extremity is flexed in the hip-joint. This is often accomplished better while the patient is sitting.

If we want to rêlax the muscles of the shoulders or the back we must do it likewise while the patient is sitting in a chair. We stand behind him and move his trunk passively forward, backward, and sideways.

Full relaxation can be generally taught in a week or less; the most difficult parts to relax are the hip-joints, shoulder-joints, and the feet, and it is to these parts that most attention should be given. We find, however, various degrees of tension in the muscles. One joint might feel stiffer than its fellow, or stiffer than we expect it to be. We then concentrate our efforts on this joint until an equal relaxation of all the muscles of the body is accomplished. Only after relaxation is fully established can we turn to the passive motions.

RE-EDUCATION

The passive motions have a very great value for re-education. We may say that they are one of the fundamental factors in the

cure. We have mentioned above that the tabetic does not trust his weak and delayed sensory impulses which he receives from the periphery, but relies more and more on his eyes. In doing so these sensory impulses, which are underlying the deep sensibility, become extinct for all practical purposes.

It is very frequent that the deep sensibility, particularly the sensibility of the joints, seems to be entirely absent. We know from analogies in other sensory spheres that a pathologic process of the degenerative kind very rarely destroys all fibers. The remaining fibers, however, are too few to be of much use; in fact, they become more disturbing than anything else, and for this reason they are entirely neglected. People who are hard of hearing neglect the few sounds which may reach their consciousness, the amblyopic eye suppresses the disturbing picture. The suppression of conception is entirely a central function due to lack of attention. I have on various occasions accentuated the necessity of blindfolding the patients during the treatment. This method of procedure has its foundation in the experiences which have been made in blind atactics. Benedict was the first who reported a tabetic who had lost his ataxia after the development of blindness. He draws the conclusions that the development of blindness had stopped the progress of the tabetic process. Cases like that have been reported a number of times, but it was left to Maloney to explain this phenomena. The disappearance of ataxia is due to the elimination of the control through the eye and the increased attention to the sensory impulses which were impaired through the disease. As long as the patient keeps his eyes open he will not perceive these weak impulses. If we want to re-educate him we must force him to relinquish the control through the eyes and concentrate his entire attention on those impulses which he receives from the joints, muscles, and tendons. The blindfolding of the patient is, therefore, the condition *sine qua non*.

The relaxation must be complete so that the patient does not mix the impulses which he receives from the joint surface with persistent impulses from the muscles or tendons. Particular attention must be given to the holding of the extremities

while moving the joint. The hands must exert constantly the same pressure on the same place, otherwise it is evident that the patient may guess the motion by drawing his conclusion from the direction of pressure on the skin.

After making a motion in the ankle-joint we shall place the fingers on the sole of the foot and the thumb on the dorsum. We shall not change position or pressure, no matter whether we make an upward or downward motion. In the state of complete relaxation this is perfectly easy. Whenever we notice that the patient uses his mucles, and one can detect it at once, we have to admonish him not to do it. I explain to the patient the working of the system, and in this way receive his co-operation, which is most essential.

Suppose the patient has no sensation at all, and we start the passive motion, for instance, in the ankle-joint, and we ask the patient if he notices anything—at first he will say no, but after repeating the same motion a number of times the patient will suddenly tell us that he feels something. We then continue with the same motion until the sensation is more marked and fixed. Then we tell the patient what we are doing, and ask him to associate the sensation with the motion. Very frequently the patient will be mistaken as to the direction; he will describe a downward motion as an upward one, and vice versa. We now teach him to associate properly. We say to him, "What you feel now is due to an upward motion, or downward motion respectively." We repeat this until the patient associates correctly. We can accomplish this to some degree even in the worst cases. One must, of course, change the rate, and examine him to be sure it is not mere guessing. The motion must be very slow and very steady, taking about five to seven seconds in each direction. No jerks or quick motions are permissible, as they may cause the sensory impulses, which may impart information to the patient which does not come from the joints, muscles, or tendons, but other parts, and thus interfere with the treatment. The motions must often be repeated hundreds of times and require a great deal of time and patience. It is for this reason that I often instruct female attendants about these

exercises. Female attendants generally have more patience than male. They are kinder and more gentle. It is evident that merely for economic reasons, to say nothing of his duties to other patients, a physician cannot spend two to three hours daily on such exercises alone.

Regarding the starting-point, I prefer, in opposition to Dr. Maloney, to begin with the small joints, and I do this for the following reasons: It is a fact that the sensibility in the larger joints is less disturbed than in the smaller ones. We find a better condition in the hip- and shoulder-joints than in the knees and elbows. This is in my opinion due to the greater difficulty to control the proximal joints with the aid of the eye than the distal ones, and for this reason the patient heeds and preserves those coming from the big joints. As a patient's instability is to a great extent due to his inability to use the feet as a steady basis, I try to improve this condition first, as the result is very striking and a source of great encouragement. I notice that highly ataxic patients become more steady after one or two treatments applied to the feet only.

Having obtained some results in the feet, we then proceed to the treatment of the knees, but we commence in every sitting again with the feet. The knees are best treated with the patient sitting on the edge of the bed or lying on the stomach. After the knees the motion in the hip is practised by flexion, extension, abduction, external and internal rotation, first with one leg only, then with both.

At the beginning only simple motions are practised. After the patient has attained the ability to describe the simple passive motions in each joint we may proceed to more complicated motions. We flex the knee and move the foot up and down—flexion of the knee and rotation in the hip, abduction in the hip, with motions in the feet, and so on in endless variations, until the patient can describe accurately what is done to him. We can then lift one leg and abduct the other, move the one toward the medial line and the other to the outside, steadily varying, so that guessing may be prevented as safely as possible.

After the patient has learned the interpretation of the sensa-

tions which are associated with the passive motions we may proceed to guided active motions, then to active and passive motions to which the patient resists, and lastly to active motions again at resistance. The sequence is not very important. One may, for instance, start with the passive motions with resistance after the guided active motions.

The guided active motions consist in simple movements, like flexion and extension, while the physician holds the parts gently and directs the motion. In this way it is possible to teach the patient the sensations which are going with a correct active motion. The motions must be steady and slow—five to seven seconds in each direction. It is advisable to count or let the patient do it.

When the patient has mastered the guided exercises we must teach him to use some strength, as it is more difficult to make a correct motion under effort than without it. For this purpose we start with passive motions, telling the patient to resist them and not prevent them.

The resistance which the patient may make should not be too strong, that fatigue may be avoided. After these passive motions, with resistance on part of the patient, we proceed to the active resistance exercises, *i. e.*, we ask the patient to do a certain motion while we resist it. Here, too, it is very important not to fight the patient, not to use too much strength, as the possibility of co-ordination is diminished in healthy individuals, but still more in atactics when the limit of strength is reached. These active resistance exercises should be particularly applied to those muscles which we found upon examination to be weak. If we see that a patient who is asked to make a certain motion without interference, we may notice that the motion is always made in a certain direction, which may indicate that those muscles that are antagonists are too weak and that the proper balance between the agonist and the antagonist is missing. If such is the case, that group of muscles which appears to be weak should be exercised in preference to the predominant. As soon as the patient shows progress in these forms of motions we may turn to more complicated motions, and we may use the method

which Frenkel has recommended, with the difference, of course, that these motions have to be done while the patient is blindfolded.

We ask the patient to cross his legs; to put the heel of the one foot on the knee-cap of the other; to lift the leg; bend it at the knee, straighten it and put it down. To put the foot on the knee-cap of the other leg and slide down along the tibia, lifting of the leg, bending of the knee, turning outside in the hip-joint, turning back. In this way various combinations increasingly complex should be made. The patient can do these exercises without any supervision and should only be advised not to overdo it. These various exercises as described above are the most important preliminary exercises, and are in many instances sufficient in connection with relaxation to give the patient sufficient co-ordination, allow him to walk without aid, and very little ataxia.

In more severe cases, however, particularly in those where the deep sensations have been lost for all practical purposes, the patient has to be taught how to use his legs. To do so we have to start with crawling on the hands and knees. The patient is provided with pads for the protection of the knees. I have found it most practical to sew these pads at the knee of the pants, which are prevented from slipping by a strap drawn across the sole of the foot. The patient should wear shoes to prevent any injury to the toes. To indicate the direction for the blindfolded patient for crawling a strip of carpet about 2 feet wide should be nailed to the floor. Narrower strips are used as soon as the patient shows some improvement. The patient is placed with the feet against the wall and each motion necessary for crawling is practised in detail. He first puts one foot forward and then backward as in the original position, then the other foot forward and back, and the same movements with the hands. As soon as he has learned to balance properly, we let him crawl across the room. His head should always be kept up. As soon as the patient has acquired a certain perfection in crawling, we go to locomotion on the knees alone.

First we let the patient balance, then we let him move one knee forward and backward while we give him the necessary support holding his hands. Gradually we may withdraw the support and let him crawl on his knees. The next step is to teach the patient to stand and keep his balance. We place him with the back toward the wall so as to give him perfect security, and stand facing him. We admonish him to abandon all fear, let his arms relax along his body, and to abstain from every effort to get support. We gradually notice that the swaying subsides more and more and that the confidence of the patient in himself increases. We then let him put one foot forward and replace it in the original position, and gradually let him walk. The walking should be slow, the steps should be short, and the patient should have sufficient security against falling without any actual aid. Putting the balance on one foot, then the other, is of great value. With progress in walking, complicated movements like walking on an incline, walking upstairs and downstairs, should be practised. I personally am against complicated movements like running or jumping, though I admit that the patient may gain confidence while walking if he is able to run. I consider the danger of falling and subsequent injury great enough as to outweigh all advantages. We do not intend to make the tabetic a sportsman. We do not expect him to race. I have seen patients who injured their legs during such exercises, and the injury interfered a great deal with their progress and recovery.

Most of the tabetics which come under our care are in such a condition that they do not need any support. In other cases, however, we find that the ligaments of the joints are overstretched and have allowed a dislocation of the various bones. For instance, we see patients whose feet show the most advanced form of a paralytic flat-foot, whose knee-joints relax to such an extent that the marked genu-recorvatum has developed. In such cases a properly constructed shoe or bandages around the leg will add greatly to the stability of the patient. In regard to the technic of these appliances I must refer to the book of Maloney. In a large majority of cases, however, a well-fitting

orthopedic shoe with some support of the arch and with strong inflexible sole will be sufficient.

The Examination of the Tabetic.—When I speak of the examination of the tabetic I do not have in mind the examination for the purpose of a diagnosis, but for a guidance in the treatment. Not every patient needs all the forms of treatment which I have described above. The majority of cases, in fact, do *not* need it, and it would be a waste of time and energy to go through the entire performance; in fact, there would be a disadvantage, as time, which could be effectively spent on some, is wasted on non-essentials.

We must first ascertain the mental state; the intelligence, its development and deterioration, the state of mind, worry, distress, disheartening irritability, hopelessness.

We have to find out under which condition he works—his efficiency, overwork, danger of losing his job, financial responsibilities.

We must then ascertain whether there is any deterioration of the eyesight. Also the condition of the bladder.

The patient is then examined in the recumbent position. We must find out whether his muscles are taut or relaxed, and the degree of stiffness or relaxation in each group of muscles, the degree of ataxia blindfolded and with open eyes. We must observe into which direction the limbs are moved preferably and try the muscular power of each group, with the object in mind, to exercise and strengthen those groups which are noticeably weaker.

The examination of the deep sensibility is particularly important, the presence or absence of joints and muscle sensibility.

It happens that the ataxia is not mainly due to deterioration of the deep sensibility, but more to psychical reasons. It is plain that in these cases even a prolonged treatment with re-education of the sensibility would not show sufficient result.

We must note these findings and regulate the treatments according to the needs of the patient. Furthermore, we must not forget to consider the rapidity of progress of the disease. It is clear that a rapid progress signifies a rapid degeneration of

the nervous tissue, and we must, as pointed out above, not overburden the patient, nor overtax his system, and prevent an aggravation of his condition. We must individualize and adapt the amount of exercises to the capacity of the patient.

REPORT OF CASES

CASE I.—A. H., admitted to the Mount Sinai Hospital May 1, 1919, admission No. 991,575. Denies lues. Had for several years dribbling of urine. Impotence since three months. Numbness of toes, progressing toward thighs and abdomen. Since four weeks loss of rectal control. Difficulty in walking for the past four weeks. Considerable difficulty in rising and sitting. Examination shows absent knee-jerks and absent Achilles' reflex. Marked Romberg. Unsteady gait with marked incoordination. There were no sensory changes. The examination showed him to be a man of marked intelligence, with no impairment of his mental state. He was a bachelor, had no particular worries, though he lived in reduced circumstances. Being a musician, he had the mind of an artist, who is not inclined to worry. His relaxation was pretty good, and the deep sensibility only slightly diminished. Skin sensibilily intact. It was evident that the case was a mild one in spite of the strong ataxia, which was due to psychologic factors, particularly to fear. He was first thoroughly relaxed, in which we were entirely successful within a day. In view of the fact that his sensations were good, we omitted the re-education of the peripheral sensory system, and began to teach the patient to practice, blindfolded, such exercises as Frenkel recommended, which are described above. After the first treatment the patient was able to stand. He began to walk after the second, and left the hospital on May 11th in such good condition that his neighbors remarked about his wonderful recovery. In view of the fact that certain symptoms like incontinence have progressed so rapidly, we may assume that it was a severe type and that the prognosis was bad. He received salvarsan injections at the hospital, which may have been very helpful. Whether the result accomplished will be a lasting one is, as far as the ataxia is concerned, doubtful, but the

very good prognosis which we made at the beginning of the treatment was verified.

CASE II.—H. H. This case was not a case of tabes, but had every symptom of a typical tabetic ataxia. A young lady, fourteen years ago, after an intensive treatment of arsenic, had lost completely her deep and nearly all her sensibilities in the upper and lower extremities. She hadn't the faintest sense of position of her extremities. She walked like a typical tabetic, with legs far apart, stamping, and closely watching her movements. In spite of that, she fell very frequently. I treated her ten years ago according to the Frenkel method, and was able to improve her walking somewhat, particularly when she had a slight support. She kept her legs closer together, did not turn her feet out so much, but she could not walk in the dark. She found herself in bed in all sorts of positions when the room was lighted. She continued to fall, but less frequently. Four years ago I began to treat her with Maloney's method. Her relaxation was fair, but not perfect. The deep sensations were nearly completely missing. The patient could not describe any position in which the upper and lower extremities were placed. It was plain that the main effort was to be directed toward re-establishment of the sensation. The prognosis was, therefore, not so good, and the duration of treatment was bound to be a longer one. The patient was put through the relaxation exercises, and she soon learned to relax completely. I then turned to re-education, but restricted my work to the lower extremities, as the necessary amount of work was enormous, and her social condition was so good that she was not expected to use her hands for earning her living. As long as she had her eyes open she could use her hands fairly well. It was therefore a decided advantage to concentrate all efforts upon the lower extremities. The patient was blindfolded about a half-hour before the sitting began and relaxed before we started with the re-education exercises. I began with the feet, moving them up and down in the ankle-joint. After twenty to thirty motions the patient reported a very slight sensation, which, however, she could not describe.

The movements were continued for about ten minutes, then the patient reported that she had two different sensations, but when told to describe the motion she continued to describe the downward motion as an upward one. The exercises were continued, and each motion was described by me—*i. e.*, up, down, up, down, etc., etc. The patient was told to associate her sensation of a motion with my description. This, of course, is difficult, just because the actual sensation is misleading. These exercises have to be repeated hundreds of times, two to three times daily, and I have therefore trained the intelligent maid of the patient how to make the exercises. After a few days she could do it as well as was necessary.

I repeat once more that I differ in that respect with some of my friends and colleagues who are using these methods. Without the proper sensation in the ankle-joint and the feet the patient will not be able to stand, no matter how good his sensation is in the knee- and hip-joint, and as it is known that the sensation in the ankle-joint is generally worse than in all the other joints, I consider it essential to lay particular stress on the re-education of the sensation in these joints. These motions in the ankle-joint were made two or three times a day. After a certain amount of progress I began to treat the knee-joint, and left the re-education of the ankle-joint to the attendant. The patient moved to the foot of the couch and had her leg dangling over the edge of the couch. The knee was straightened and bent by placing my hand under the heel and moving the leg very gradually up and down. The motion of these exercises were continued until the patient could describe correctly the movement that was made. I then took the hip-joint. Abduction, adduction, flexion, and extension, as well as rotation was practised. After that we combined motion in the hip, knee, and foot. The treatments were, of course, to be given daily by myself and twice by the attendant—in all, three treatments a day. After a few weeks we began to let the patient crawl blindfolded across the floor, which she was able to do very well. We had no difficulty in teaching her to walk on her knees, an experience which is quite common, for the reasons mentioned above—that

the hip-joint is the one in which sensation is the least affected. After three weeks decided progress was noticeable—the patient knew during the night in what position her legs were, and could correct it if necessary. After about two months we started to teach the patient to walk blindfolded. In cases like this, where the relaxation is good and the sensation badly impaired, the re-education exercises in bed are far more important than the walking exercises, as naturally the improvement of the sensation is the most important foundation for the acquisition of the co-ordinated movements. We began the walking exercises, starting with standing erect against the wall, and the motions as I have described above. The treatment was fairly successful and only lasted about three or four months. The patient can now walk without any support; her walk is still somewhat abnormal, but she has no difficulty whatever in locomotion during the day at home as well as on the street, and she has not much difficulty in walking in the dark except when walking upstairs.

CASE III.—A. G., forty-five years, patient in the Neurological Department of the Mount Sinai Hospital. He was atactic for some years. His mentality was somewhat affected. He gave the impression of being a taboparetic. He had little ambition, and was not very much interested in earning a living for himself. The examination showed that his deep sensation was fairly good, but the patient kept his muscles so stiff that it was impossible to relax him, and his ataxia was very marked. It was evident in this case that the prognosis would be good, depending ultimately only on the progress of the disease and on the complication with paresis. This man did not receive any re-education, but merely relaxation, and it was possible within one week to put him on his feet and make him walk with only a mild degree of ataxia. The patient discontinued the treatment, as he was not particularly interested in his recovery.

CASE IV.—A. F. is a patient weighing 220 pounds. His muscles are very strong. He is an uneducated individual, but his mentality was not impaired and he is very ambitious.

The relaxation was pretty good, but there was complete absence of the deep sensibility and of the sensibility of muscles and tendons. The ataxia began only seven weeks ago, but was so high that it was impossible to keep him on his feet, even with the help of two men. He had no conception of the position of his feet, and most every attempt to put him on his feet was of no avail because he would throw his legs about wildly. Even when the patient was in bed he was not able to turn or get on his knees. The treatment had to be directed toward re-education. The outlook was good, as the muscles are strong and the patient ambitious, but the time necessary for treatment will be a long one. We began with the motions of the feet as usual. The patient did not respond at all for the first few minutes, not knowing that anything was being done to him, but when we forced his attention on his feet, and continued with the motions, the patient could soon distinguish motions made in the ankle-joint. When we started to move the knee-joint the patient did not perceive any motion either, but regained the sensation very soon. While he retained the sensation in his knee-joint, he lost it from day to day in the ankle-joint. After one week, however, we could always get a correct answer on passive motion in the ankle, knee, and hip. When we turned to the active exercises it was seen that the patient was lacking muscular sense; that he did not know which muscles were in action, and it was very difficult to teach him how to make active flexion and extension in the ankle-joint. This is very important. A patient who does not know which muscles work or to which muscles he is sending impulses cannot be expected to make co-ordinated movements. This inco-ordination, however, was particularly marked in the ankle-joint, while other muscles acted fairly well. The patient was therefore taught to practice the Frenkel exercises for himself blindfolded, and we strived particularly to teach him active and resisted movements. This case tends to prove the importance of an accurate analysis of each case. It is evident that in a case like this we have to pay much more attention to the training of the muscles, as they are the foundation for our movements. The re-education of the sensation of the joints was

soon successful, and we were able to teach the patient enough, within one week, to enable him to turn quietly, with closed eyes, on his stomach, to get on his knees, to crawl on his hands and feet, and even to kneel. If we allowed him to open his eyes he could kneel without swaying. Two weeks after the beginning of the treatment we were able to put the patient on his feet and let him stand, of course, supported by one man on each side. It is necessary in these cases to remain in this stage for quite a time. I should not advise the forcing of the treatment.

I want to draw attention again to the fact that the actual work is easy if only the factors on which the walking depends are favorable. A patient who learns to perceive his sensations while he is standing and who can distinguish the joint sensation from muscle sensation will not need much training in walking —they, naturally, follow. The treatment of the patient was continued in the same way, with very good results. The patient had strong muscular power, and it was natural that with the gaining of the control of these muscles the result must be a good one.

I do not intend to describe the treatment of those very severe cases which are not only bedridden through their incoordination but also through their mental inertia, or such patients who are suffering from diseases of the joints. These patients offer a variety of problems, and it would be impossible to impart the knowledge of the treatment to a practising physician by a mere article. Such patients must be treated in institutions where they are under permanent care. Cases as I have described above can be treated by every physician, and the results are sometimes startling. I want to emphasize once more the importance of a thorough analysis of the symptoms for the treatment as well as for the prognosis.

CLINIC OF DR. I. W. HELD

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A DISCUSSION ON THE SPLENOMEGALIES

Historic Review; the Spleen as a Blood-making Organ and an Organ of Blood Destruction; the Influence of the Spleen on Blood and Blood-making Organs; the Spleen as a Hemolymph Gland; the Interrelation of the Spleen and Liver; the Relation of the Spleen to the Anemias; the Interrelation Between Spleen, Liver, Lymphatic Glands, and Bone-marrow; Splenomegalies in the Acute and Chronic Infections and Parasitic Diseases; Splenomegalies with Disease of the Hematopoietic System; Splenomegaly in Hemolytic Icterus; Gaucher's Splenomegaly; Banti's Splenomegaly; Etiology and Pathologic Anatomy; Pathogenesis; Symptoms and Course; Differential Diagnosis; Prognosis and Treatment; Polycythemia Vera or Osler-Vaquez Disease; Splenomegaly Due to Stasis and Malignancy.

THERE are many etiologic factors and a still greater number of pathologic conditions concerned with the physiologic pathology of the spleen. It has always been and is still a question, in a great many instances, as to when an enlarged spleen is primary or secondary. It is even difficult for able clinicians with most modern methods at their disposal to arrive at a definite diagnosis.

An organ the physiology of which is still so obscure does not lend itself so readily to a study of physiologic pathologic conditions. Through the efforts of Howell and Janeway here, and Krehl abroad, we endeavor to approach our interpretation of disease through knowledge of the physiology of an organ. Although our knowledge at the present time of the spleen in these varied relationships is still meagre and incomplete, yet a

brief review of what has been definitely determined and even some of the debatable problems on the study of the physiology of the spleen will be discussed in order to make us understand more intelligently the splenomegalies.

Historic Review.—Even the ancients knew that a splenectomy was compatible with life. Paracelsus goes so far as to say that the spleen is dangerous to the organism. Splenectomy was practised by the Romans to improve the wind of their runners. The most diverse and absurd opinions existed until the middle of the 19th century as to the function of the spleen. F. Kraus states that the spleen went through a mythologic era of its own. No less a physiologist than du Bois Reymond began and finished his chapter on the spleen in this wise: "Now we come to that important subject, namely, the physiology of the spleen, about which we know nothing." Notwithstanding such pessimism from so eminent an authority, progress on the function of the spleen was not retarded, and the clinician, ever striving to establish exact diagnosis based on proper etiologic factors, using such means as more exact studies of blood made available by Ehrlich, and from pathologic studies of spleens extirpated from patients suffering with severe splenic trauma, pernicious anemia, hemolytic icterus, or Banti's disease, was able to throw a great deal of light on the physiology as well as the physiologic pathology of the spleen.

The Spleen as a Blood-making Organ.—The normal spleen contains neither erythroblasts nor myelocytes. The follicles of the spleen form small, medium-sized, and large lymphocytes, endothelial cells, and other cells with rich protoplasm of an endothelial habitus. In part these latter cells belong to the group of large mononuclear cells of the blood. Whether these pulpa cells, also called splenocytes, are further developed lymphocytes, or are an offshoot of the endothelial cells, has as yet not been decided. The cells just mentioned give a positive oxidase reaction, indicating that they are closely allied to myeloid tissue. Jochman and Müller found a tryptic ferment in these pulpa cells. The granulocytes and the erythroblasts produced in the spleen during embryonic life disappear from among those

cells formed by the normal spleen. In diseases accompanied by a stimulation of the hematopoietic system, as in myelogenous leukemia, pernicious anemia, lymphatic leukemia, and even in many forms of severe secondary anemia, there occur in the follicles of the spleen large numbers of myelocytes, erythroblasts, and granulocytes at the expense of the follicles, the latter almost entirely disappearing. In lymphatic leukemia the lymphocytes are found in unusually large numbers at the expense of the pulpa. In multiple myeloma the myeloid tissue is a compensatory product for all the myeloid tissue in the bone-marrow.

The Spleen as an Organ of Blood Destruction.—The most important rôle attributed to the spleen in the blood metabolism is its property of destroying the formed elements in the blood, blood-platelets as well as the red and white cells. The end-products of the destroyed red cells are carried by the blood-stream to the splenic vein, thence through the portal vein into the liver, where the liver cells convert them to bilirubin. The liver elaborates the broken-down elements of the other cells into energy-producing substances.

The Influence of the Spleen on the Blood and Blood-making Organs.—The study of the blood changes and the changes in the blood-making organs after extirpation of the spleen furthered our knowledge of the relation of the spleen to other blood-making organs. In animals the experimental studies of Kerrlaff under Ehrlich are epoch making. He found in guinea-pigs a leukocytosis in the form of lymphocytes and enlarged glands persisting for a year after splenectomy. During the second year eosinophilia was present. In the human being the removal of the pathologic spleen is frequently followed by a neutrophilic and later lymphocytic leukocytosis, and finally an eosinophilia appears. It is interesting to note that a few observers noted bone pains following splenectomy, such symptoms being, of course, due to bone reaction. Asher and Sollberger report polycythemia after splenectomy, and H. Hirschfeld and Weinart make the important observation that after extirpation of the healthy as well as the diseased spleen Howell-Jolly bodies are persistently found in the blood. In one case they found such

bodies nine years after splenectomy. This demonstrates the fact that after removal of the spleen there is an abnormal function of the bone-marrow interfering with the denucleation of the erythrocytes. The spleen is evidently a regulator of this denucleation.

That the activity of the bone-marrow is evidently influenced by removal of the spleen is illustrated by the experiments of Asher and Sollberger, who showed that the withdrawal of small quantities of blood from splenectomized animals does not lead to such a high degree of anemia as it does in normal animals, but sometimes even polycythemia is produced. They explain this occurrence to be due to the hyperactivity of the bone-marrow. It is quite likely that the relation between bone-marrow and spleen is governed by a hormone. While red blood-cells are being destroyed in the spleen the bone-marrow continuously forms new cells to keep pace with the destruction. It is quite probable that the end-products of the destroyed red blood-cells stimulate the bone-marrow to the formation of new red cells. After the removal of the spleen with the cessation of the destruction of the red blood-cells one would expect the hyperactivity of the bone-marrow to cease, but the reverse is true. The bone-marrow is spurred to further increased hyperactivity as indicated by the appearance of blood crises with the appearance of embryonal forms of red cells, so that one of the hormones of internal secretion must be sought for as a regulating factor.

Resistance to hypotonic salt solution is increased after splenectomy. This was tested from blood leaving the spleen by the splenic vein, and is demonstrated clinically in cases of hemolytic icterus after splenectomy. In this disease, where there is found a lowered resistance of red blood-cells to hypotonic salt solution, there is found after splenectomy an increased resistance which is explained most likely by the fact that the bone-marrow quite probably produces cells of greater resistance.

The spleen is a storehouse for iron; 5 per cent. of the iron substance is stored up in the spleen for the future body economy. Splenectomized animals fed on iron-free substances develop anemia much more quickly than the normal animal.

The Spleen as a Hemolymph Gland.—Just as the spleen retains the old and ready to be destroyed red and white blood-cells, so does it also serve as a storehouse where micro-organisms lodge (typhoid and plasmodium). The spleen plays the same rôle for the blood as do the lymphatic glands for the lymph-vessels, hence the appropriateness of the title of this paragraph suggested by Holly. The destruction of the blood-cells in the secondary anemias, and the deposition of their elements in the spleen, as well as the presence of great numbers of bacteria in the infections, explains the enlargement of the spleen in these diseases. Since the spleen is the organ where bacteria, in the infections, lodge in such great numbers and are there destroyed, it has been rightfully considered as the place where the first important antagonism to the bacteria takes place. W. J. Mayo considered the tonsils and other lymphoid tissue, such as the appendix and spleen, as vaccinators, where phagocytosis was stimulated as a result of the passing through and lodgment of great numbers of bacteria. Clinicians of centuries ago considered enlarged spleens in the febrile condition of good prognostic significance. Research workers found evidence contrary to this idea, in that splenectomized animals injected with pathogenic organisms resisted infections as well as the non-splenectomized animals. F. Kraus has pointed out, however, that conditions are different in animals and are not always analogous to human beings suffering with infectious diseases, so that experimental evidence is not altogether satisfactory proof. The fact that splenectomized animals resist bacterial infection does not lessen the importance of the spleen as a vital organ assisting in the usual resistance of infection. That certain organs, like tonsil, appendix, or spleen, can be removed with impunity does not mean that these organs are functionless. It is an established fact that organs of vital importance have compensatory structures performing similar functions. There is very little data as yet available as to how the removal of a pathologic spleen influences the course of an infectious disease in a human being.

The importance of the spleen in relationship to malignant growths has been studied by Braunstein experimentally, and

later by others. They utilized the fact that the spleen is seldom the seat of malignant disease by feeding splenic extracts to patients suffering with carcinoma. Braunstein transplanted carcinoma cells into splenectomized and normal animals, and whereas the former invariably developed carcinoma, the latter did not. He also fed splenectomized animals with implanted carcinoma and splenic extract. He found that they developed either no carcinoma at all, or very small solitary growths.

The Interrelation Between Spleen and Liver.—It has long been known that the spleen influences bile formation in the liver. That bilirubin is a derivative of hemoglobin is a well-proved fact. Just as bilirubin is elaborated in the liver, so is the spleen the place where the red blood-cells are destroyed, and the remnants of these broken-down blood-cells are transported to the liver through the splenic and portal circulation where the transformation from hemoglobin into bilirubin takes place.

Splenectomized animals produce a paler bile, according to Pugliese. The same author showed experimentally, and it is now confirmed, that in splenectomized animals destruction of blood-cells takes place in the bone-marrow and in the stellate (Kupfer) cells of the liver. In animals with a spleen the product of the disintegrated hemoglobin reaches the liver by the portal and splenic veins in a concentrated form; in splenectomized animals these products pass through the circulation, and therefore reach the liver in a diluted form, and bilirubin is produced much more slowly. The strongest proof that the spleen has such important influence on the production of bilirubin, both as to quantity and the length of time necessary for its manufacture, is the fact that splenectomized animals stand poisons like toluylendiamin and pyrodin better than those with a spleen, and that the former produce a paler bile. The explanation of Pugliese was just mentioned.

Joannowitz explains the greater resistance of the splenectomized animals to poisons differently. Toluylendiamin exercises its hemolytic influence *in vivo* only and not *in vitro*. In the living organism there must be a substance under the influ-

ence of which the above-named poisons cause hemolysis. According to the author just named the place of origin of such a substance is in the liver. The work, however, is not fully confirmed. In fact, the late A. Pappenheim does not accept this theory at all, and advances the rather plausible hypothesis that blood-poisons increase the destructive property of the spleen to the red blood-cell, and splenectomy removes this effect.

The spleen has been compared by Rowntree to the glomeruli of the kidney, and the liver to the tubules, the one straining out degenerated cells, micro-organisms, and poisons, and the other acting on the material brought to it. The interrelated pathologic condition of the spleen and liver follows closely the interrelation of function.

The Relation of the Spleen to the Anemias.—Such anemias as result from growths of the spleen, or the large spleen accompanying infectious diseases, parasitic diseases, or abscesses of the spleen, are easily explained as similar affections of other organs, likewise cause anemias of equal degree. The anemias, on the other hand, that are met with associated with structural changes in the spleen, not due to tumor or infection, are of unusual interest. Some enlightened and intelligent explanation as to the relation the spleen bears to such anemias has been offered in the last few years.

Primarily, such anemias are the outcome of an exaggerated blood destruction in the spleen. For some time the bone-marrow accommodates itself to make up for this change, which explains the frequent intermissions of well-being of patients afflicted with such anemias. Eventually the cell productive property of the bone-marrow becomes exhausted and the anemia progresses to a fatal termination. This is certainly the mode of origin of the anemia accompanying hemolytic icterus. In pernicious anemia the blood destruction in the spleen must be a very important factor. This is to a great extent proved by the fact that urobilin becomes markedly diminished both in the urine and stool after splenectomy in this disease.

Eppinger explains the increased hemolysis in the spleen in pernicious anemia in the following way: "The walls of the

arteries carrying the blood from the follicles to the pulpa undergo hyaline changes. Some of the vessels become narrowed down to a point of obliteration. On account of this the erythrocytes reach the pulpa directly through the capillaries, where they are found in unusually large numbers, whereas the venous sinuses are almost empty. The pulpa, according to Eppinger, is the seat of sensitization of the red cells." The ingenious and painstaking work of the author just named, although not confirmed by such pathologists as Hanseman and Benda, deserves a great deal of consideration, as it has a practical application.

It is now known and accepted that splenectomy in those specific conditions above mentioned, if not permanently relieving the condition, at least brings about a temporary intermission quicker than any method hitherto known. It is probable that the pathologic picture described by Eppinger is an effect rather than a cause of pernicious anemia, and the primary cause is still veiled under the enterogenous or other vague infections or toxic agents. The value of his teachings are, however, not minimized, for the clinician has long recognized that the removal of the effect often removes the cause.

The removal of an enlarged syphilitic spleen in a luetic, who previously did not yield to specific treatment, responds most readily to antisyphilitic remedies after splenectomy. In the same sense splenectomy should be followed by all other known therapeutic agents in combating the ravages of pernicious anemia.

It is known that the bone-marrow plays an important rôle in pernicious anemia, and that the degree of the anemia is not only dependent on the destructive property of the spleen, but also on the degree with which the production of the red cells goes on in the bone-marrow. Analogous with the studies of internal secretions, Eppinger speaks of hypersplenia and asplenia. Pernicious anemia and hemolytic icterus represent the former, polycythemia, the latter. According to Hirschfeld and Weinart, the presence of Howell-Jolly bodies in the erythrocytes after splenectomy is one of the signs of asplenia. Hirschfeld also speaks of a dysfunction of the spleen in Banti's disease, and

according to that author the anemia, leukopenia, and the spleen depends on the diminished new blood formation in the blood-marrow as well as the increased blood destruction in the spleen. The influence of the spleen on the bone-marrow is lost.

The Interrelation Between Spleen, Liver, Lymphatic Glands, and Bone-marrow.—This interrelationship is a well-established fact. The histologic and functional changes which are brought about in the liver, lymphatic glands, and bone-marrow after splenectomy can be divided into the following groups:

A. Such that indicate stimulation.

B. Compensatory changes.

C. Signs showing absence of spleen.

A. The stimulating effect of splenectomy on bone-marrow is indicated by the neutrophilic leukocytosis, later eosinophilia and mononucleosis, following the splenectomy.

B. The compensatory changes are indicated by the lymph-glands becoming enlarged. Lymphocytes increase in numbers. The histologic changes in the liver and bone-marrow are likewise compensatory.

C. The persistence of Howell-Jolly bodies, lighter colored bile, occasional transient polycythemia, diminution, and even disappearance of iron in the usual places of deposit, all testify to the absence of the spleen. These changes are, of course, very transient in nature.

The influence of the spleen on trypsin, pepsin, and intestinal peristalsis has been studied by Schiff, Hayem, Gross, and Zulzer. This field is fascinating and still open to experimental work before clinical information of much value can be derived therefrom. Zulzer's studies on the intravenous injection of a hormone (named by him "hormonal") derived from the spleen in the treatment of intestinal stasis and postoperative intestinal paralysis was hailed for a short time, but subsequent trials by many competent clinicians have failed to stamp this as a remedy of the value claimed by Zulzer. During the years 1911 and 1912 it was tried by us in several cases without encouraging results. In fact, in 2 cases the anaphylactic phenomena which presented themselves after injection were most alarming.

Hirschfeld summarizes the functions of the spleen as definitely determined by experimental proof in the following fashion:

1. The spleen is a blood-making organ, and in health it produces lymphocytes and large mononuclear cells. In leukemias, anemias, and infectious diseases it takes on the added function of forming red blood-cells and granulocytes.

2. The spleen destroys the red blood-cells and prepares the hemoglobin for elaboration by the liver into bile.

3. It is concerned in the iron metabolism.

4. It is a regional lymph-gland of the blood; it not only filters the lymph, but serves as a graveyard for red and white cells, as well as the blood-platelets. All foreign substances circulating in the blood, especially bacteria, are detained in the spleen and to some extent made less injurious. The spleen also produces protective agents against bacteria.

5. It is a regulator of the erythroblastic function of the bone-marrow.

6. According to some authors it influences the digestive ferment action.

7. The regenerative quality of the spleen and the occurrence of supernumary spleens are established facts.

In "The Spleen and Anemia" Pearce, Krumbhaar, and Frazier summarize the results of splenectomies on dogs as follows:

Secondary anemia appears, mild or severe, reaching its highest stage one to one and a half months after splenectomy; then repair begins, and is complete after three or four months as a rule.

There is increased resistance to hopotonic salt solution, hemolytic serum, cobra venom, and mechanical shaking.

There is lessened tendency to hemoglobinuria, jaundice, and sometimes an absence of jaundice after the introduction of hemolytic agents.

The anemia is irregular, and the red blood-cells diminish in number before the hemoglobin is decreased.

There is leukocytosis after the operation sometimes reaching as high as 38,000, and consisting entirely of polymorphonuclears. There is later lymphocytosis and eosinophilia.

Fatty yellow bone-marrow is transformed into red bone-marrow. There is no evidence that this is compensatory. They believe that in the absence of the spleen the bone-marrow takes up the function of storing and elaborating the old blood pigment.

The lymph-nodes after splenectomy show an increase in endothelial cells, which suggest that in the absence of the spleen the function of forming red blood-cells and phagocytic cells, normally a minor function of the lymph-nodes, now becomes highly developed in these structures.

The metabolism of iron, fat, and nitrogen is not disturbed by splenectomy.

Before discussing the splenomegalies from the clinical aspect a few remarks on the method of examining the spleen may not be amiss.

Inspection is the least important of all methods, only being of academic interest. In thin individuals with large spleens inspection may reveal the position and size of the spleen.

Palpation is the most important method. The soft infectious spleen should be palpated lightly, as it is readily displaced and thus missed. The hard spleen is easily accessible to palpation. The finding of a notch in the mass examined characterizes it absolutely as spleen. Sometimes the spleen may be so large that the notch rests under the left lobe of the liver, so that it becomes necessary in such cases to inflate the stomach and thus separate liver from spleen. The enlarged kidney and mesenteric tumors are differentiated from spleen by inflation of colon, the spleen being always anterior to the colon.

Often the spleen presents a pulsating tumor, so that one can mistake it easily for some other mass. This especially happens in some cases of aortic insufficiency, and marked left ventricular hypertrophy, and was noticed in tricuspid insufficiency by Manges.

Auscultation becomes useful in diagnosing the acute perisplenitis by eliciting friction.

x-Ray.—When stomach and colon are inflated, or the newer method of introducing oxygen intraperitoneally is employed the outline of the spleen becomes very definite.

Puncture of the spleen in cases of malaria, leukemia, kala-azar, or tumors is a very valuable diagnostic method.

Splenomegalies in the Acute Infections.—Most of the infectious diseases are accompanied by enlarged spleens. Especially is this true in childhood, when minor infections as well as metabolic disorders lead to enlarged spleens. Even mild colitis in children and especially the summer diarrhea cause an enlarged spleen. The enlargement is interpreted as an expression of resistance on the part of the individual. The pulpa is unusually filled with the causative bacteria, which are caught there and made more or less inactive. Streptococci and staphylococci lodge there in large numbers, and although pus-producing in other organs, they seldom form pus in the spleen. This is another evidence of the bactericidal and defensive property of the spleen. Under very rare conditions, however, the pus-producing organisms do cause abscesses in the spleen.

The parasites of kala-azar and malaria always have their main habitat in the spleen, whereas the Spirochæta pallida and the tubercle bacilli are often found there. Each of these produce characteristic pathologic changes, gumma, tubercles, and interstitial changes depending entirely on the causative organism, and thereby producing the large spleen. The myeloid metaplasia in the pulpa and the finding of phagocytes in certain of the infectious diseases is regarded as a sign of heightened resistance brought about by the spleen. It would be germain to this discussion to mention all the infectious diseases in which an enlarged spleen is found. In typhoid, the large, soft spleen remains as long as the disease lasts, and its persistence means that the infection still remains even though the symptoms are lessened. The spleen in this particular disease is always enlarged, but escapes the clinician's palpation because of its unusual softness. In this condition, trauma, subsequent rupture, and abscess are more common than in any other disease causing splenomegaly.

Febris recurrens, acute miliary tuberculosis, bacterial endocarditis, during the active and bacteria-free stage, are all accompanied by enlarged spleens.

Weil's disease deserves mention because of its association with a large spleen. The disease was described by Weil in 1866, and often occurs in small epidemics. It has symptoms characteristic of any infection, but its most diagnostic features are jaundice, splenomegaly, and acute nephritis. There is usually an acholic stool and bile in the urine, although in some cases these latter features are missing. There may be a slight hemorrhagic tendency. The disease runs a course of two to three weeks and usually terminates favorably.

Splenomegalies in Chronic Infections and Parasitic Diseases.—Of the chronic infections, tuberculosis should be mentioned first. An enlarged spleen accompanies tubercular lymph-granuloma and tuberculosis of the liver.

Primary tuberculosis of the spleen, with characteristic tubercles and giant cells, deserves special mention. It is not as uncommon a disease as is generally supposed. A. Pappenheim was especially impressed with the fact that in one year he had 4 authentic cases, proved by autopsy, where only the spleen was the seat of tuberculosis. He summed up the clinical picture in the following way: It occurs during all ages, 2 of his cases were between thirty and forty, 1 occurred during childhood, and 1 after fifty. Judging from the literature, the most common age incidence is between thirty and forty. Unlike all other splenomegalies, not even excluding tumor of the spleen, this disease is accompanied by pain and discomfort and marked uneasiness. The pain and discomfort is referred to the left hypochondrium. Progressive weakness and emaciation are more marked than the anemia which exists. The anemia may be progressive, but even a polycythemia may exist. They ascribe this special feature to a dysfunction of the spleen. The spleen may feel nodular on palpation and may sometimes assume an enormous size. Because of the splenic vein thrombosis and its extension to the liver, the disease in the late stage is accompanied by tuberculous cirrhosis of the liver, ascites, and quite often pressure effusion into both pleural cavities, simulating polyserositis. With ascites alone, it becomes impossible to differentiate this disease from Banti's, and with effusion into the pleural cavities, circulatory embarrass-

ment, advanced anemia, pressure on the femoral vessels, with accompanying edema of the lower extremities, as well as glandular enlargement, the disease has often been mistaken for Hodgkins' lymph granuloma.

Splenomegaly in congenital lues is a constant feature. Often enough gummata and spirochetes are found in the spleen. In acquired syphilis the spleen may become large, accompanied by a secondary anemia, with a mononucleosis and leukopenia, so that it is mistaken for a Banti's until a Wassermann proves otherwise. In fact, until the era of the Wassermann reaction Banti classed these cases as those belonging to the group described by him.

In malaria the spleen often remains enlarged throughout life, and sometimes attains such size with coincident anemia that it is difficult to differentiate this condition from splenomegalies accompanying diseases of the hematopoietic system. Even puncture of the spleen often fails to reveal the real identity of this disease. During the past war a number of methods were introduced to accelerate the passage of the plasmodiums from the spleen into the blood, when splenic puncture and ordinary blood examination failed to reveal the malarial organism. Active exercise and the application of faradism over the spleen have been advocated by some, while the most successful method is the intramuscular injection of 1 mgm. of adrenalin, and the examination of the blood-smear for the malarial organism after a forty-eight-hour period.

Splenomegalies with Disease of the Hematopoietic System.—The splenomegalies in some of the primary anemias is only of interest as far as pernicious anemia is concerned. In this disease the spleen is always enlarged pathologically, although palpation often fails to reveal it. The relation of the spleen to pernicious anemia, and the work of Eppinger in this regard, has already been mentioned.

Both in leukemic as well as in the aleukemic systemic diseases the spleen attains considerable size. In the non-leukemic diseases of the blood-making organs that today go under the misnomer of pseudoleukemia, whereas they should be called

lymph-granulomas in their various aspects, like Hodgkins' lymph-granuloma, Sternberg's lymph-granuloma, Kundrat's lymph-granuloma, an enlarged spleen is usually met with. In fact, the spleen is so prominent a sign in the group of diseases that it was named splenic anemia, or anemia lianalis.

It is now known that in these leukemic conditions the splenic tissue is converted into myeloid tissue, and the blood-picture may be myeloblastic or myelocytic. As there are three types of myelocytes, so it is possible to get any of the varieties in the blood-picture. Recently, Shapiro of Patterson, added one case of eosinophilic myelocytic leukemia to the few cases already described. The disease is usually chronic, although acute leukemias often occur. In the acute type the spleen does not attain the characteristic large size.

Griffin just recently reported another case of eosinophilic polymorphonuclear leukemia. His case showed splenomegaly, enlargement of superficial lymph-glands, and a white count that revealed 73.5 per cent. eosinophils and 24 per cent. polymorphonuclear leukocytes. This patient had edema and ascites. Splenectomy was performed, and the patient lived for three years after. Eosinophilia was constantly present.

It is of clinical importance to make brief mention of the myeloblastic type of leukemia first described by Türck. Up to that time this form of leukemia was confused with subacute lymphatic leukemia, because it often begins with bleeding gums and tonsillitis. Most cases described, and one of our own cases, began with disease of the gums, necessitating the patient's visit to the dentist. A tooth was extracted, and subsequently the dentist was sued for malpractice because of symptoms simulating sepsis which developed later. The picture was at first complicated because the blood showed an aleukemic type, only 3000 white cells being found, of which 90 per cent. were myeloblasts. It may be mentioned that the myeloblast was at that time not differentiated from the large lymphocyte, and the diagnosis of subacute aleukemic lymphemia was made, and confirmed by E. Libman and R. Ottenberg. Now, of course, the oxydase reaction makes the differential diagnosis between these two cells

easy. The hemorrhagic tendency is not so marked in the myeloblastic as in the acute lymphatic leukemia.

The aleukemic myeloid leukemia is usually diagnosed by the fact that there are myelocytes and other evidences of bone-marrow reaction in the blood. A normal differential count makes diagnosis very difficult. Hirschfeld quotes a case where the entire course of the disease was marked by a normal differential count, and only splenic puncture revealed the true nature of the disease. Sometimes a severe anemia accompanies the disease, and because of the megaloblastic cells in the blood pernicious anemia is thought of. The absence of nervous symptoms and achylia in the presence of a large spleen should tempt one to do a splenic puncture to clear up the diagnosis. Hirschfeld quotes another case which presented an advanced state of hemolytic icterus accompanied by myelocytes in the blood. This, together with a large spleen, made the differential diagnosis between a primary myeloid leukemia and hemolytic icterus difficult. The persistence of the lowered resistance of the red blood-cells to hypotonic salt solution, as well as the frequent colicky pains in the right hypochondrium, the presence of urobilin and absence of bile in the urine, made the diagnosis of hemolytic icterus more plausible in spite of the presence of myelocytes.

Very recently Chauffard and Bernard described a case that they named "pernicious anemia with jaundice" that very much resembles the case quoted above. This illustrates how far the splenomegalies and their associated diseases are from being solved. The fact that such mixed pictures may occasionally occur to make differentiation difficult as to what the primary disease may be suggests to us the explanation that the interrelation of the hematopoietic organs is an intimate one; and that disease of one may so disturb all other hematopoietic tissue as to take on characteristics of more than one disease.

Splenomegaly in Hemolytic Icterus.—In both the familial congenital type, as well as in the acquired form of hemolytic icterus, one meets with a considerable enlargement of the spleen.

Pathologically, the spleen presents marked congestion of

splenic pulp and splenic sinuses. Pigment deposits and macrophages are increased. The follicles, capsule, and trabeculæ show no change at all. In this disease there is an unknown toxic agent in the spleen exercising an injurious effect on the red blood-cells, causing their destruction. That explains the reason for finding in the spleen, besides the enormous dilatation of the blood-vessels, the filling of the same with an increased number of dead red blood-cells and increased blood-pigment. That the increased destruction of the red blood-cells is responsible for this symptom-complex is further proved by the fact that the removal of the spleen causes a disappearance of the symptoms, and likewise after splenectomy the lowered resistance of the red blood-cells to hypotonic salt solution is changed so that it becomes normal.

The cardinal symptoms of this disease are chronic enlargement of spleen, existing with an acholuric, non-obstructive jaundice. There is a secondary anemia of a chlorotic type, the color-index being low. The anemia is frequently paroxysmal in character and varies in intensity.

Increased blood destruction is indicated by increased urobilin in the urine and changes in the blood. The red cells show diminished resistance to hypotonic salt solution, and there is an increased number of reticulated cells with vital staining. In the acquired Hayem-Widal form of this disease the anemia is graver, and the jaundice is not so marked. The phenomenon of auto-agglutination of the red blood-cells takes place in this special form.

The congenital Chauffard Minkowski type presents a more "icteric than sick" patient.

Some of the variations from the typical hemolytic icterus picture are:

1. Those cases where acholuric jaundice and splenomegaly have existed, with polycythemia instead of anemia.

2. Evidence of increased blood destruction, but no change in the resistance of the red blood-cells.

3. Evidences of increased blood destruction, but no jaundice present.

The blood-picture may so strongly resemble pernicious anemia that it is often difficult for well-trained clinicians to differentiate one from the other. The following differential points ought to guide one. The spleen in pernicious anemia is rarely as large as in hemolytic icterus. The resistance of the red blood-cells is not diminished as a rule, and there is usually a leukopenia and a relative lymphocytosis, whereas in hemolytic icterus there is a neutrophilic leukocytosis. Myelocytes are rather a frequent finding in hemolytic icterus, whereas macrocytes and megaloblasts, often seen in pernicious anemia, are the exception in hemolytic icterus. Increased quantities of urobilin in the urine and blood-serum are also diagnostic features of hemolytic icterus. The presence of achylia gastrica, and neurologic symptoms referable to spinal disorders, are characteristic of pernicious anemia. It should also be mentioned that the intermittency of the icterus and occasional attacks of pain in the right hypochondrium are important diagnostic signs of hemolytic icterus.

Jaundice accompanying Hanot's cirrhosis with a large spleen is never associated with diminished resistance of red blood-cells. There is usually bile in the urine, and there is never such a high degree of secondary anemia.

The splenomegaly in Von Jaksch's anemia will only be mentioned as one of the conditions in which an enlarged spleen is found. A clinical discussion belongs to the domain of pediatrics.

GAUCHER'S SPLENOMEGALY

Gaucher's large cell "splenomegaly" was first described by him in 1882 as a primitive epithelioma. Brill, Mandlebaum, and Libman, whose pathologic and clinical studies are most creditable and conclusive, showed that these large cells developed simultaneously from spleen, bone-marrow, and lymph-nodes. The characteristic large cells with their small eccentric nuclei block the sinuses of the spleen and lymph-nodes. The pathologic picture is one easy to recognize. During life diagnosis was made possible by splenic puncture, first done by E. P. Bernstein. Splenectomy in this case was performed by Henry Roth, and is reported in the Archives of Pediatrics, 1914, p. 340.

An acute form of Gaucher's disease is described by Nieman, Jahrb. für Kinderheilk., 1914, v, 79, p. 1.

The etiology is unknown. Endogenous toxins, splenic enzymes, and infections have been promulgated as causative factors. None is as yet accepted. McMannus and Ludden claimed to have produced the disease experimentally by feeding animals with cholesterin. The symptomatic description is best found in Brill and Mandlebaum's papers in the American Journal of Medical Science, 1905 and 1909. A brief résumé of their complete description is given here.

The disease begins insidiously before the thirteenth year, and pursues a very chronic course. The average duration is about twenty years. It is often met with in several members of the same family. Early in the disease there are no symptoms, but later progressive weakness with hemorrhagic tendencies, particularly in mucous membranes and skin, leads the patient to the physician. Fatal hemorrhages are not the rule. Pappenheim mentions the case of a fatal esophageal hemorrhage which occurred two years after splenectomy. The most prominent symptom is the enlargement of the spleen, which may approach the size of the spleen reached in myelogenous leukemia. Blood changes are not characteristic, but there is usually a leukopenia. The liver is enlarged, but there is no enlargement of the lymph-nodes. Jaundice and ascites are rare.

The skin shows a peculiar yellow brown discoloration, and yellow wedge-shaped thickenings of the conjunctiva are seen on both sides of the cornea.

Hermann, Roth, and Bernstein report that of 9 cases splenectomized, only 3 recovered. Spontaneous cures are out of the question. Splenectomy should always be advised, but when we consider, as was pointed out by Brill, Mandlebaum, and Tebrinan, that the large cells originate simultaneously from bone-marrow, lymph-nodes and spleen, we realize how futile splenectomy alone is in combating this disease. Treatment subsequent to splenectomy should be along such therapeutic lines as radium and *x*-ray.

It is of great interest that a case shown by W. H. Scholtz in

1912, before the Berl. Klin. Sez., was that of a patient who died of diabetes and had a high degree of lipemia. The spleen showed a small number of follicles and almost entire disappearance of pulpa. The cells resembled very much the endothelial cells of the type of Gaucher. Since then Lutz reported a similar case in Ziegler's Beiträge, vol. 58, and Marchand, in the Munich Med. Woch., No. 1915. In connection with the cases just cited it may be of interest to recall again the experiment of McMannus and Ludden quoted above.

BANTI'S SPLENOMEGALY

We will have to discuss this somewhat in detail, because, of all affections associated with splenomegaly and anemia, not one has been subject to such controversy as the symptom-complex described by Banti. A number of authors furnish pathologic and clinical evidence that Banti's disease is not an independent entity; a large number of authors are of the opinion that it is an independent affection. We must take the stand that "veritas in medio consistet." If we can rule out splenomegaly with anemia of known etiologic factors like lues, malaria, thrombosis of splenic and portal veins, atrophic cirrhosis of liver, primary tuberculosis of the spleen, then the diagnosis of Banti's disease is absolutely justifiable. So much more so are we duty bound to diagnose the case properly, as a splenectomy during the first stage of this disease is a very successful method of treatment.

Under the name "Banti's disease" we understand a condition which is still named by some "splenic anemia," but runs a characteristic course, is favorably influenced by splenectomy, and has well-defined anatomic changes in the spleen.

Etiology.—A definite cause is unknown. Banti himself considered an infection the primary cause. All efforts, however, to demonstrate this infection were without avail. Gibson, in Quart. Jour. of Med., 1914, described 6 cases where he found a streptothrix, but later observations by other authors, and experiments to produce the disease in animals with streptothrix, failed to confirm Gibson's work. Enterogenous toxins and trauma to the spleen have been considered as predisposing factors.

Banti himself, in his 50 cases, found it more frequent in women than in men. It occurs most often before the age of thirty-five. Banti's youngest case was twelve years, his oldest, fifty-five. Very often the infantile habitué is mentioned in common with this disease.

Pathologic Anatomy.—The spleen is, as a rule, smooth and hard. It is often four or five times the normal size. Perisplenitis is occasionally met with, splenic infarcts are rare. The main changes are brought about by a progressive increase in the stroma at the expense of the parenchyma. This is the process named by Banti "fibrodynia." The changes in the pulpa are diffused. Few of the follicles are left unchanged. The disease of the follicles begins in the central artery, and the end-stage is the conversion of the entire into a sclerotic knot, until the follicles gradually disappear. This is a very important argument in favor of this disease being an independent pathologic entity. The chronic sclerotic endophlebitis of Banti are changes in the intima of the splenic vein which often extend to the portal vein. The liver shows no changes during the first stage, and only begins to become involved during the second stage as a result of the just mentioned endophlebitis. Later a hyperplasia of the connective tissue of the interlobular branches of the portal vein takes place, and during the third stage a true cirrhosis of the liver occurs, a condition impossible to differentiate clinically from atrophic cirrhosis of the liver.

Siderosis is never met with. The bone-marrow appears red, the lymph-nodes are unchanged, and during the third stage the organs show dilated veins and signs of a hemorrhagic diathesis.

Pathogenesis.—Banti in his original communication expresses himself as follows: 'An infectious agent of unknown origin localizes itself in the spleen and brings about a fibrodynia." This agent probably gets to the spleen by the arterial circulation, because the changes in the arterioles of the follicles are the most prominent features. On account of this infection toxic agents form in the spleen, which he named "splenotoxins." These toxins bring about changes in the blood-making organs, later in the splenic and portal veins and liver. The anemia is not of a hemolytic nature, because all landmarks of hemolytic anemia

are missing. The urobilin that may sometimes be found in the urine, and which made Umber consider the disease analogous to hemolytic anemia, is usually a very late manifestation—when the liver is co-affected.

We have already mentioned above that it is still disputed as to whether Banti's disease is a definite entity or not. Work by recent investigators like Moschovitz, Symmers, and his pupils, as well as Naunyn, disclaim the identity of Banti's disease, because some of the pathologic changes described by Banti were not found by them, and other lesions that were also originally described by Banti were found in splenomegalies associated with other definite diseases. As non-pathologists we cannot argue this question with authority, but as already intimated, it seems to us important to lay stress on the point already made, that there are cases that cannot clinically be interpreted as anything else than Banti's disease. The fact that every pathologist does not find what Banti described seems to us no argument, because organs examined pathologically depend upon their findings at what stage of the disease the organs were examined. We realize that Banti described his cases before the Wassermann era, and before his work was subjected to criticism, and, therefore, he included many cases that today he would exclude as typical Banti's. Banti's anemia is rightfully of splenogenic origin, and develops on the basis of a dysfunction of the spleen. The myelotoxic element is evident by a diminution of red blood-cells in the bone-marrow. Whether this element is produced in the spleen by its structural changes, or whether different toxic agents exist that exercise a deleterious effect on the spleen, bone-marrow, and liver, is not as yet ascertained. We must still make the painful confession that the etiology of Banti is veiled in obscurity.

A few remarks should be made as to the name "splenic anemia," still confused with Banti's disease. This term was first employed by Griesinger. It seems to us that it is a term as much abused as the name "pseudoleukemia." Even as brilliant an authority as Osler mentions Banti's disease in connection with splenic anemia. Often today at the bedside the findings

of a large spleen with anemia is passed off with the diagnosis of splenic anemia, a term which only tells us that there is a palpatory spleen and that anemia exists. Our advanced clinical and laboratory methods that have clarified and facilitated our diagnoses so well forces us today to confess that we cannot interpret some large spleens with anemia at all, or that we are face to face with some definite entity. Naunyn, for instance, not accepting Banti's as a definite entity, calls this condition hypersplenic liver cirrhosis, because during the stage of the cirrhosis of the liver it is hard to differentiate these conditions. We are still to mention, however, that even clinically as well as pathologically there are differences between the two diseases.

Some authors speak of Banti's as a splenic pseudoleukemia. The word "pseudo" in medical literature is objectionable enough as to exclude the name. Another name, "splenic lymphadenosis," has been suggested. The objection to this is that, as a rule, the other lymph-glands are not affected, and why a generalized lymph-glandular disease should localize in the spleen, persist there, and invade the liver, and still leave out the lymph-glands, is not easy to perceive. On the other hand, such diseases like Gaucher's splenomegaly and hemolytic icterus, which are likewise splenic diseases, behave just like Banti's in that they produce changes in the bone-marrow, invade the liver eventually, but do not invade the lymph-glands.

Symptoms and Course.—Banti divides the disease into three stages:

First stage: The spleen grows gradually and can even attain an enormous size. There are, as a rule, no symptoms unless the anemia advances rapidly. When weakness, malaise, loss of desire or ability to work, dyspnea on exertion, cold extremities, often a slight tendency to a hemorrhagic diathesis begins to appear.

Second stage: This period is characterized by enlargement of the liver. The skin of the body has a dirty yellow, sallow appearance, the conjunctiva is discolored, the urine becomes concentrated, albumin and granular casts are almost the rule, urobilin is still the exception, although there may be liver changes. The anemia becomes more marked and the tendency to hemor-

rhage becomes very prominent. Hemorrhages from stomach and rectum are particularly prone to occur, and sometimes even fatal hemorrhages take place.

Third stage: The disease now presents symptoms simulating atrophic cirrhosis of the liver.

Blood changes were mainly studied by Banti, Senator, and others. During the first stage a chlorotic type of anemia is characteristic, the red blood-cells being decreased in number later on in the disease. In many cases in the second stage a hemoglobin of 50 to 60 per cent. is encountered with a normal red count. When even the red blood-cells are diminished in numbers the morphology and staining qualities of the red cells are not disturbed. Normoblasts are never found and leukopenia is the rule. According to Banti, the following blood-picture is characteristic. A moderate hypoglobulism, sometimes even a transient hyperglobulism, and always oligochromia. The color-index is low, there are no nucleated reds, no leukocytosis, no myelocytes, there exists a tendency to leukopenia and there is an absolute lymphocytic leukopenia.

Differential Diagnosis.—The diseases that offer the greatest difficulty in being differentiated from Banti's are the following: First and most important is atrophic cirrhosis of liver. A prolonged history of alcoholic indulgence, also the history of prolonged gastric symptoms, including nausea and vomiting, speak for atrophic cirrhosis. The facies of the patient is also characteristic, the dilated venules of the nose and the smooth, velvety skin, make us more sure that we are dealing with a primary liver condition. In early cirrhosis the symptoms precede the palpatory findings, and during this stage the liver is certainly more palpable than the spleen. Urobilin is found early in atrophic cirrhosis, and if found at all it is a late manifestation in Banti's which speaks for the hepatogenic origin of the former and the splenogenic origin of the latter. During the later stages of atrophic cirrhosis, when ascites is a prominent factor, it is more difficult to differentiate it from the third stage of Banti's, but even then the secondary anemia and the blood-picture mentioned above is the exception in cirrhosis of the liver. The hemorrhagic

tendency is not so marked in cirrhosis, although the first hemorrhage may prove fatal. The hemorrhages in Banti's occur often—one hemorrhage rarely proving fatal, although it sometimes does.

Lues may fully simulate Banti's and is only differentiable through a positive Wassermann. In case the Wassermann is negative, and still we suspect lues, it may be mentioned that a luetic splenomegaly, with involvement of liver, anemia, and ascites is much more progressive than Banti's. Evidence of some glandular enlargement is also present in this luetic condition.

Thrombosis of the portal vein is not so rare as it is difficult to diagnosticate clinically. From the differential standpoint the etiologic facts are of great importance. As a disease primarily originating in the vein proper it is usually secondary to a phlebitis elsewhere. It is more common secondary to pressure from without, caused by such conditions as primary lues of the liver with extension to the periportal structures, or as one case cited by Ewald, where there was a periphlebitis portal luetica, glands in lymph-granuloma, Hodgkins' abdominalis pressing on the portal vein, pancreatic and gastric tumors, sometimes the extension of periduodenitis, and other diseased conditions of the mesenteric glands.

The symptoms depend entirely as to whether obstruction is complete and rapidly progressive without giving time to the collateral circulation to establish itself. What interests us here are those cases where splenomegaly and ascites are very marked features. In such cases where etiologic factors cannot help us out, it is often an impossible task to make a differential diagnosis. It may be of diagnostic importance to note that ascites is the first symptom noticed by the patient, and that the gastro-intestinal symptoms are much more marked than in Banti's, especially the tendency to diarrhea, with brownish, bloody stools due to the dilated veins in the intestine. Otherwise the other signs of a hemorrhagic diathesis are missing. Splenic vein thrombosis is a constant accompaniment of Banti, particularly in the second and third stages, and is a frequently associated condition with primary portal vein thrombosis.

Sometimes the lymph-granuloma of the Hodgkins' type, especially where we have mediastinal or abdominal Hodgkins', gives rise to difficulty in differential diagnosis. A case we had occasion to observe was one in which splenomegaly, large liver, ascites, and a marked anemia were present. The following points made us lean toward the lymph-granulomatous condition: An effusion into the chest due to pressure, unilateral edema of the extremities due to pressure of glands on the femoral vein, and marked periods of intermission so common in Hodgkins' and rare in Banti's. Although the glandular enlargement was not a marked feature, it was still more marked than one finds in Banti's, and, finally, an excision of the gland showed the pathologic picture so characteristic of Hodgkins'. Furthermore, during the stage of ascites in this latter disease there is usually the Pel-Ebstein fever curve, a polymorphonuclear leukocytosis, and there may be a transient eosinophilia. Pruritis, a common feature in Hodgkins', is unknown in Banti's.

Occasionally the aleukemic myelogenous leukemia offers difficulty, but the anemia, especially in the morphology and tinctural property of the red cell, as well as the presence of nucleated reds, and the cachectic type of anemia, the absence of ascites, and the presence, usually, of glandular enlargements, ought to be of diagnostic aid and differential value.

Naunyn speaks of the so-called splenogenic cirrhosis of the liver instead of Banti's disease, and asserts that pathologically cholangitis and cholangiolitis lead to lesions similar to those of Banti's. The clinical evidence, however, seems too meager for his view to be accepted. In the first place, the cases mentioned by Naunyn show only urobilinuria and early jaundice, and it seems to us that his group of cases belongs to the infection type of cholangitis rather than to Banti's disease.

Prognosis and Treatment.—The disease usually runs a course anywhere from ten to fifteen years. If diagnosed early and splenectomy is then carried out, prognosis ought to be favorable. On the other hand, cases recognized in the second and third stage have an absolutely bad prognosis, because the advanced changes in the liver, secondary changes in bone-marrow, and

secondary hemorrhages from various parts of the gastro-intestinal tract are such that the removal of the primary cause can no longer effect improvement, not to speak of a cure. Of 2 of our cases who were splenectomized, 1 died a few years later from a severe hemorrhage from an esophageal varix, and shortly before exodus developed subcutaneous emphysema due to esophageal perforation, and the other patient died two years following splenectomy from uncontrollable gastric hemorrhage.

Treatment other than splenectomy narrows itself down to palliative measures. Transfusions, intramuscular injections of cacodylate of soda, and appropriate hygienic measures are, of course, available and should be used.

POLYCYTHEMIA VERA OR OSLER-VAQUEZ DISEASE

In 1892 Vaquez described a condition of hyperglobulism with cyanosis, which he believed due to an overactivity of the blood-forming organs. Later Senator, Cabot, McKeen, and Russell described similar cases. It was in 1903 that Osler described a group of cases with chronic cyanosis, polycythemia, and enlarged spleen as a definite, new clinical entity. The cause of this condition is still unknown. Koranyi and Bence have suggested that the disease is due to a lessened power of the red blood-cells to absorb oxygen, thus necessitating a greater number of erythrocytes to meet the demands of the system.

Pathologically there exists a true plethora. Intense hyperplasia of the bone-marrow, a myelomatous rubra, and an enlarged spleen with histologic changes indicative of chronic passive congestion make up the rest of the picture. According to Eppinger this is an example of asplenia.

The polycythemia may be relative in which the condition is due to a diminution in quantity of the plasma of the blood, or, true, in which there is an actual increase in the number of blood-corpuscles. Relative polycythemia is common, most often caused by loss of liquids, sweat, diarrhea, and increased diuresis. Narrowing of the pylorus, with dilatation of the stomach, has been known to cause polycythemia. Chronic cyanosis is a common feature in organic heart disease, particularly in con-

genital malformations, chronic myocarditis, tricuspid lesions, and adherent pericardium. In emphysema and long-standing pulmonary tuberculosis the cyanosis is apt to become especially marked.

The cyanosis in polycythemia attracts most attention; it is usually most marked about the face and hands. The cyanosis may be constant, but varies greatly in intensity. There is no respiratory distress with the cyanosis. Some cases do not present this cyanosis for the following reason: If the capillaries are full, and the blood flow slow, cyanosis predominates, whereas if the current is rapid an arterial color is prominent. The conjunctivæ are usually diffused and the eyes may appear prominent.

The viscidity of the blood is greatly increased, looks unusually dark, and the drop is thick and sticky. A great increase in the number of red blood-cells is usual and is the special feature of this disease. Cabot described a case in which the red count was 12,000,000. The percentage of hemoglobin is high, in some cases reaching 165 per cent., but is relatively low, the color-index being lower than 1. The leukocytes are moderately increased, ranging about 10,000. The occasional presence of myelocytes has been repeatedly seen in the blood-smear.

The spleen is moderately enlarged, in some cases the enlargement is very marked, reaching the navel in 4 of Cabot's cases.

The subjective symptoms are all referable to disturbances in the central nervous system. Christian has pointed out that a failure to keep the nervous symptoms of this disease in mind may lead to mistaken diagnosis, and sometimes to cerebral operations, with the idea that the symptoms were the result of brain tumor.

Vertigo, buzzing, whistling in the ears, paroxysms of dizziness, headache, pain and prickling sensations in the extremities, loss of consciousness, and thickness of speech are some of the more common symptoms. It is because of these symptoms that the patient seeks the doctor. Some symptoms are even so focal in character as to lead to diagnosis of brain tumor.

These nervous symptoms are due for the most part to sec-

ondary vascular circulatory disturbances, hemorrhages and thrombosis taking place.

Recently Wartline quoted a case of chronic cyanotic dyspnea and erythemia, with a red count of 7,000,000 to 8,000,000. The interesting finding postmortem was arteriosclerosis of the pulmonary artery and all its branches, with extreme dilatation of the right breast. The microscopic examination revealed the presence of a typical syphilitic mesarteritis, and also changes in the stomach wall of a syphilitic character.

Before leaving this special entity it may be mentioned that the cases described by Gaesback, with high blood-pressure, undoubtedly belong to the group just described.

Prognosis, so far as life is concerned, is good, but recovery in the true polycythemia is unknown. Treatment is very unsatisfactory. Frequent venesections were advised by Senator, and transient favorable results were reported. But inasmuch as venesection has a tendency to stimulate red blood-cell formation, and to increase the viscidity of the blood, it is at its best a very doubtful remedy. Benzol, *x*-ray, and radium treatment have also been recently recommended. Treatment of the nervous system with appropriate hydrotherapeutics, restricted work, restriction of meat in the diet are other therapeutic measures.

SPLENOMEGALY DUE TO STASIS

Stasis due to a decompensated heart deserves our first attention. As a rule it causes no independent symptoms, although Eppinger and Primbrams attribute the secondary anemia in decompensated cardiacs to the destruction of red cells in the diseased spleen. They base their assertion on the finding of large quantities of urobilin in their patients' stools. This finding of a large spleen is not a frequent occurrence in decompensated cardiacs, and when a large spleen is found associated with valvular disease bacterial endocarditis or infarcts to the spleen should be sought for.

Another important disease with a large spleen because of stasis is that due to thrombosis of portal or splenic vein, or, what is more commonly the cause, cirrhosis of the liver. A

clinical discussion has already been given under the differential diagnosis of Banti's disease.

SPLENOMEGALIES DUE TO MALIGNANCY

Malignant tumors of the spleen causing splenomegaly are very rare as primary diseases, and metastatic growths in the spleen, especially carcinomatous, are unusually rare. In fact, Schmidt, in his famous book on abdominal tumors, makes the statement that when we can palpate a tumor in the left hypochondrium, and can safely state that it is an enlarged spleen, the idea that we are dealing with a malignant intra-abdominal tumor can be discarded. The fact that metastatic growths do not usually occur in the spleen prompted Braunstein to suggest splenic extracts as a therapeutic agent in combating carcinoma.

Lewin, Weidener, Oser, and Primbrams are the few who report finding malignant nodules in the spleen. Those malignant nodules deeply seated in the spleen without changing the contour of it are still rarer. In general carcinomatosis and sarcomatosis, with metastases throughout the entire body, an involvement of the spleen may occur.

Of the rare primary new growth of the spleen the origin was found in connective tissue and vessels, stroma, and parenchyma. From the stroma originate fibroma, endothelioma, sarcoma, and angioma; from the parenchyma spring the lymphosarcoma. Primary sarcoma of the spleen occurs in the young, grows very rapidly, forms a nodular tumor, deforms the normal contour of the stomach, and very often becomes adherent to surrounding organs. Due to pressure on lymph- and blood-vessels early ascites may result. Since metastases is a very early manifestation, early diagnosis and splenectomy is the only hope. Endothelioma and primary lymphoscarcoma is undoubtedly rare.

Hemangioma of the spleen is closely allied to the cysts, and they are sometimes so small that they cause no splenic enlargement. As far as can be determined from the literature, none were diagnosed during life.

Aneurysm of the splenic artery causing splenomegaly has been mentioned, but was also not diagnosticable during life.

Cysts sometimes cause an enlarged spleen. They are divided into parasitic and non-parasitic cysts. The non-parasitic cysts, according to Hirschfeld, are:

1. Those due to softening of tumors, tubercles, gummas, bleeding into splenic parenchyma of traumatic origin.

2. Real cysts, lined with endothelium, found most frequently postmortem. The large cysts of the spleen are mostly hemangiomas. The contents of these cysts depend entirely as to whether hemorrhage has taken place into them, when their contents will be quite bloody; otherwise, the contents are serous or clear. These cysts are found more often in women than in men. The diagnosis is quite difficult, but where there is a history of trauma, followed by temperature, without tenderness and leukocytosis, and on palpation a smooth fluctuating tumor in the splenic region can be made out, the diagnosis of cyst of the spleen is probable. Puncture for diagnostic purposes should be avoided.

Of the parasitic cysts, the echinococcus cyst is most important, but even this is very rare, occurring only in 4 per cent. of the cases. Diagnosis can be established by finding evidence of echinococcus elsewhere in the body, by complement-fixation, and eosinophilia.